ajh

ATDEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

CIRCULATORY SYSTEM DEVICES PANEL

Monday, April 7, 1997

9:36 a.m.

Room 020B
9200 Corporate Boulevard

MILLER REPORTING COMPANY, INC.
507 C Street, N.E.
Washington, D.C. 20002
(202) 546-6666

ajh

Rockville, Maryland

PARTICIPANTS

Julie A. Swain, M.D., Chairperson
John E. Stuhlmuller, M.D., Executive Secretary

VOTING MEMBERS

Anne B. Curtis, M.D.
Francis B. Gilliam III, M.D.
Tony W. Simmons, M.D.

CONSULTANTS APPOINTED TO TEMPORARY VOTING STATUS

Jeffery A. Brinker, M.D.
Gabriel Gregoratos, M.D.
Ronald M. Weintraub, M.D.

CONSULTANTS

Jacqueline Simmons, M.D., M.P.H.
(Chairman, General Hospital Advisory Panel)
George W. Vetrovec, M.D.

CONSUMER REPRESENTATIVE

David A. Gooray, M.D.

INDUSTRY REPRESENTATIVE

Jean A. Goggins, Ph.D.

FDA

Thomas J. Callahan, Ph.D.

C O N T E N T S

P R O C E E D I N G S

Call to Order

DR. SWAIN: Good morning. I would like to call to order the Circulatory System Devices Panel Meeting. We will first have a reading of the conflict of interest statement.

Conflict of Interest Statement

DR. STUHLMULLER: The following announcement addresses conflict of interest issues associated with this meeting and is made a part of the record to preclude even the appearance of an impropriety. The conflict of interest statutes prohibit special government employees from participating in matters that could affect their or their employers' financial interests.

To determine if any conflict exists, the agency reviewed the submitted agenda and all financial interests reported by the committee participants. It was determined that no conflicts exist.

In the event that the discussions involve any other products or firms not already on the agenda for which an FDA participant has a financial interest, the participants should exclude themselves from such involvement and their exclusion will be noted for the record.

With respect to all other participants, we ask, in the interest of fairness, that all persons making statements

or presentations disclose any current or previous financial involvement with any firm whose products they may wish to comment on.

Class I financial interests include compensation for time and services of clinical investigators, their assistants and staff in conducting the study and appearing at the panel meeting on behalf of the applicant. Class II interests include direct stake in the product under review, for example, inventor of the product, patent holder, owner of shares of stock, and Class III interests include owner or part owner of the company.

DR. SWAIN: Thank you.

I would like each panel member to now do an introduction with their name, where they are from and their area of specialty.

DR. T. SIMMONS: Tony Simmons, Bowman Gray School of Medicine, Wake Forest University, cardiology, electrophysiology.

DR. J. SIMMONS: Jacqueline Simmons, no relation to Dr. Tony Simmons. I am a general internist from Miami, Florida, practicing internist. My specialty is preventive medicine and public health. I am an adjunct assistant professor at the University of Miami.

DR. WEINTRAUB: Ronald Weintraub, cardiac surgeon,

Beth Israel Deaconess Hospital in Boston.

DR. VETROVEC: George Vetrovec, Medical College of Virginia, Virginia Commonwealth University at Richmond, Virginia, interventional cardiology.

DR. GOORAY: I am David Gooray from Washington, D.C. I am in general cardiology.

DR. GOGGINS: Jean Goggins, Medical Director, Medox Medicals, and industry representative to the panel.

DR. GREGORATOS: Gabe Gregoratos. I am a clinical cardiologist, University of California at Davis.

DR. BRINKER: Jeff Brinker, Johns Hopkins.

DR. GILLIAM: Rosie Gilliam from Richmond, Virginia, cardiology and electrophysiology, private practice.

DR. CURTIS: I am Anne Curtis from the University of Florida in Gainesville, Florida, cardiologist and electrophysiologist.

DR. SWAIN: I am Julie Swain, University of Kentucky, cardiovascular surgery.

The voting members for today are Anne Curtis, Rosie Gilliam, Dr. Sethi, who is not here yet, and Tony Simmons.

The consultants appointed to temporary voting status for this meeting are Jeff Brinker, Gabe Gregoratos,

and the alternate, Ron Weintraub. I am not sure what alternate means.

DR. STUHLMULLER: In the event of the unexpected absence of a voting member.

I need to read one statement for the record.

It is appointment to temporary voting status. Pursuant to the authority granted under the Medical Devices Advisory Committee charter, dated October 27th, 1990, as amended April 20th, 1995, I appoint the following people as voting members of the Circulatory System Devices Panel for this meeting on April 7th, 1997: Jeffery A. Brinker, M.D., Gabriel Gregoratos, M.D., Ronald M. Weintraub, M.D.

For the record, these people are Special Government Employees and are consultants to this panel. Under the Medical Devices Advisory Committee, they have undergone the customary conflict of interest review and have reviewed the material to be considered at this meeting. Signed by Elizabeth E. Jacobson for D. Bruce Burlington, M.D., Director of Center for Devices and Radiological Health, dated March 31st, 1997.

DR. SWAIN: I would also like to mention that as Dr. Goggins said, she is the industry representative, and Dr. Gooray is the consumer representative.

Do we have any old business?

[No response.]

DR. SWAIN: Lacking that, we will go to new business, which is the open public hearing on Premarket Notification Application K963904 on the Heart Alert, Inc., Cardiac Event Recorder device.

This is the open public hearing part here, traditionally the company presents.

DR. STUHLMULLER: They are going to present initially as part of the open committee discussion. During the open public hearing, the North American Society of Pacing and Electrophysiology has requested time to speak, and Alan Morgan and Cynthia Tracy, M.D., will present for NASPE at this time.

Open Public Hearing

DR. TRACY: Good morning. Thank you.

I apologize. I almost missed this. I got twisted around on Redland Road and circled this building for about half an hour.

I am here on behalf on NASPE, the North American Society for Pacing and Electrophysiology. There is the summary statement which was sent from NASPE to you. I believe all of you have a copy.

NASPE is a professional organization of physicians and scientists.

DR. SWAIN: Cindy, excuse me. Could you declare a conflict of interest or financial status with this company?

DR. TRACY: Since I don't know what the company is, I have no conflict of interest, no financial interest in any of this. I am simply as a representative of the Professional Society of Electrophysiologists and Scientists dealing with heart rhythm disturbances.

Transtelephonic monitoring is a type of monitoring device that physicians typically will use to survey patients who have some type of transient symptom that might suggest that they are having a heart rhythm disturbance, so it is the type of patient that you are concerned about who has fainting spells or near fainting spells where you can't catch it on a routine electrocardiogram or a physical exam or a 24-hour Holter monitoring, so this is the type of device that you might place on a patient and send them for two or three weeks with the unit in place.

It is often self-activated by the patient. The devices that are currently available have several different types, ranging from ones that the patient activates themselves to ones that record automatically.

It is a fairly sophisticated system and the key to making the device work is having good contact between the patient and the physician. So, anytime a patient is sent

out, the device is prescribed, an order is called in by the physician to the company or to their own hospital that is surveying the results of these devices, saying alert me if patient so-and-so has three beats of ventricular tachycardia or a pause greater than two seconds.

So a very distinct prescription is called in for the patient, and the patient is given very clear instructions as to the phone number to contact to make a transmission after they have recorded, for example, on their wrist device. They then call in the results of that recording.

The recording then, if it meets the criteria that the physician has predetermined as being potentially life-threatening or serious to warrant contact, the physician is then contacted by telephone and by fax transmission with the electrocardiogram that was transmitted by the patient.

So the key thing here is the good contact between the patient and the physician in order to make this thing work.

The concerns that NASPE raised about an over-the-counter device like this are several fold. There is nothing stated here as to what the contact will be, who will determine the guidelines to say this is a dangerous

rhythm or this is not a rhythm that the patient is transmitting, what level of sophistication does the person receiving the transmission have in terms of interpreting the results of the transmission.

What might be a very benign rhythm for one patient may be a potentially life-threatening rhythm for another patient and vice versa. So, there is no assurance here that anybody with any degree of sophistication is going to be receiving their transmission.

Once the transmission is received on the over-the-counter device, then, what happens, does a physician out of the blue get a telephone call and say your patient, Joe Smith, who you may not have seen in 12 years, just called in with five beats of supraventricular tachycardia?

So, the main problem that NASPE sees with this thing is a problem of contact and knowing how to interpret the data when it comes in.

The other issue that we have concern over is the quality of the transmission that will be made by the device. Many times you, with the patient, have to go through two or three different types of transtelephonic monitors in order to come up with one that works for the patient.

A simple wrist recorder may not work on one

patient, whereas, a loop recorder where they hook up electrograms to the chest may work. So this flexibility is needed, a very carefully defined prescription is needed in order to be sure that you are going to get adequate information for caring for the patient.

The other, on sort of a personal level, I am not sure how a patient would handle this type of monitor. This is kind of a scary thing, this monitor. If you call in to a technician who doesn't know you and says, yes, you had three beats of something, patients are going to be very, very frightened just out of context to know that they have something there that the monitor has picked up, whereas, it may be a completely benign thing, and if I, as a physician, have prescribed the device, I would say, look, you are going to transmit premature such and such, don't worry about it, it means nothing, but to out of the blue get contact from a technician saying that you have something on your monitor, I think would be fairly terrifying for a number of people.

So, I think that is just more of a personal, maybe not a NASPE level concern.

So, just to summarize then, our concern is one of continuity of care, contact with the patient, and the quality of the transmissions that will be made with this device.

DR. SWAIN: Thank you.

The next presentation is Alan Morgan.

MR. MORGAN: I am Alan Morgan, health policy analyst for the North American Society of Pacing and Electrophysiology.

DR. SWAIN: Financial class?

MR. MORGAN: Excuse me?

DR. SWAIN: Your financial class?

MR. MORGAN: Financial class?

DR. SWAIN: Are you related to this company in any way?

MR. MORGAN: Absolutely not. Absolutely not.

DR. SWAIN: I think we will have your presentation. Then, we will have questions of the panel members to both you and Cindy.

MR. MORGAN: Very good. Dr. Tracy covered the main points that NASPE had although the financial end of it, we have no relation to this company. We don't know who this company this, and that presented a unique dilemma for us in commenting on this because we could only comment on the broad-based concerns that we would have with such a device.

In such and not seeing the specific application of this company, NASPE would suggest that perhaps a pilot study might be a better way of looking, going forward with this to

addressing some of the concerns that we are not really sure of. Perhaps in the application itself, it addresses this, and a pilot study would not be necessary, but that was one of the general concerns that our members had of looking at this issue without any specific information from it.

As I said, Dr. Tracy presented our comments, and we will have written comments. I believe you may have them. If not, we will provide them to you.

Thank you very much.

DR. SWAIN: Do the panel members have questions for Dr. Tracy or Mr. Morgan?

DR. GREGORATOS: A comment. I appreciate NASPE's input. I think NASPE probably had been at a disadvantage because you probably just received the general announcement, a letter, a generic letter from the agency, you have not seen the specifics.

So, some of your comments will be addressed, but many of your comments are very similar at least to mine and probably other members of the panel, so we will see how it plays from here on.

DR. BRINKER: There are a couple members of NASPE on this panel. It probably should be obvious to you all. One of the questions that we are going to have to separate out is the issue of patient entitlement to make their own

decisions about health care, perhaps independent decisions, and whether that is appropriate, at least for this class of physicians.

Now, my understanding from your statement is that that is not the issue that is being entertained, and the issue that you are really entertaining is, is there some information that can be supplied to you showing that this mood of arrhythmia detection is safe for the patient, has some sort of effectiveness, and that if that demonstration could be made, even though it takes the individual physician out of the loop, that NASPE would have no problem with this issue, and if data, for instance, from a study, let's say, in another country in which this form of option were available and showed that it was effective and people weren't dying of anxiety when the found out that they had three beats of something, that would assuage NASPE's concern?

DR. TRACY: I would be very interested in seeing data that might have been gathered on the use of this type of an instrument. Cardiac rhythms are a fairly unique category of disease or an entity, it is not something that is easy for the patient to determine the significance thereof.

A diabetic who has a home blood sugar monitor

knows that when they have a blood sugar of 220 or 240, that it is not quite right. A person at home with a structurally normal heart who has vaguely mediated paroxysms of atrial fibrillation may not realize that that is a benign disturbance.

It is very difficult for a patient to make the type of decision regarding what needs to be done, I would think, based on what is recorded.

Now, the majority of transmissions, as many of you know, that we get, will be very benign findings, but it does take often a lot of time and a lot of reassurance, and perhaps some background studies on the patient to reassure them that that is nothing that needs to be treated, nothing to be concerned about.

So, I think it would be -- I am not so much concerned that people are going to be dropping dead from untreated disturbances. I am more concerned about the overdetection of things that might not need to be treated.

So, I would be interested to see the results of anything that you have like that, but I think some of these concerns would still exist in terms of the quality of care that we want to provide patients in this country.

DR. BRINKER: Well, that is a critical issue, and the issue is, is there a threshold by which NASPE would be

satisfied that this is a reasonable approach, or is the mere fact that this takes the consulting physician, and the consulting physician-patient relationship out of the picture. Really, at least that is a screen. Is that something that NASPE is set against?

DR. TRACY: I have to defer, at least to some extent, on the global NASPE policy, but it has been NASPE's feeling that cardiac rhythm disturbances are best treated by cardiologists and electrophysiologists, and not by lay people.

DR. BRINKER: That gets right to the point. What kind of, for instance, pilot study would you want if the bottom line is we are not going to be happy with anything less than a physician-directed arrhythmia management, so I think that issue has to be clear from your policy point of view.

DR. TRACY: Right.

DR. SWAIN: Are there any other questions? Ron.

DR. WEINTRAUB: How are you going to defend this when you see this the Washington Post, that this very safe device, which really has no down side in terms of specific patient health or safety, has been knocked by NASPE or voted down by the panel because NASPE is a guild for cardiologists with EP training, and they don't want to be taken out of the

loop and lose all their fees and reimbursement, you know, how are you going to answer that?

DR. TRACY: I think it is clearly not an answer of reimbursement. It is clearly an answer of the difficulty of interpreting the significance of cardiac rhythms in any patient population.

I think there are times where a physician is needed in order to make a determination that something is benign or something is not benign. It is too much of a burden, I believe, to place on the individual to interpret the results of their transtelephonic monitor.

I don't know who the receiver is on the other end. I don't know what level of technician or physician support is on the other end, but it is too much of a burden to place on --

DR. WEINTRAUB: Well, I am the patient. I will take the burden. You know, I am a strong fellow and I believe in the American way and being independent and taking responsibility for my own care. What is wrong with that, that is a harmless device?

DR. TRACY: It may be a harmless device just as a blood sugar monitor is a harmless device.

DR. WEINTRAUB: But I can do my blood sugars at home.

DR. TRACY: And have a physician-directed therapy after you do the blood sugar. It is not possible for a individual patient to determine what the appropriate therapy or lack of therapy is based on the results of any test, and this is a very difficult area to manage. Cardiac arrhythmias is a very difficult area to manage, and it is not a reasonable thing to have the patient determine what must be done.

DR. WEINTRAUB: Well, even the experts, I mean they didn't do so well by Reggie Lewis. You know, maybe I will do better on my own.

DR. TRACY: Maybe you would.

DR. WEINTRAUB: I mean I think this is the kind of thing that -- you know, I am sympathetic with your point of view, and I take care of cardiac patients, too, and they certainly have high levels of anxiety, and I understand the objection, but this is the kind of public response we, NASPE, FDA may get if we take it out of the patient's hands.

DR. TRACY: I think that is reasonable to expect are response like that, but I think that this is a fairly educated population that would even desire such a monitor, and hopefully, we would be able to educate them further as to the need for a link to the physician.

I don't know how this thing was envisioned to fit

into the health care scenario, but just to leave a monitor in a patient's hand is just too scary to think about for that patient.

DR. SWAIN: Dr. Simmons. Jacqueline, you can start first.

DR. J. SIMMONS: I was just wondering what questions you would pose in your pilot studies.

DR. TRACY: I haven't seen anything more about this device than what was presented to NASPE, and it is fairly brief. I think the questions that would have to be answered at least immediately is who is receiving the transmissions, who does the quality assurance on the transmissions, what contingencies are there if the transmissions are inadequate, who gets notified if there is an abnormal rhythm disturbance and what kind of 911 backup is there with the device.

Most of the companies that we use through prescription use will automatically call 911 if there is a lethal rhythm disturbance, so what kind of emergency backup is available. Does it meet the same standard that the currently available devices have.

DR. SWAIN: Tony Simmons.

DR. T. SIMMONS: Just a couple of quick questions. Number one, you know, I am a member of NASPE, and certainly

I didn't get polled on this. I mean what part of NASPE is responding to this?

MR. MORGAN: That would be the NASPE Health Policy Committee and the NASPE Executive Committee.

DR. SWAIN: If you answer questions from the back, you need to speak in the microphone because this is being recorded. So, Cindy can just repeat that.

DR. TRACY: It was the Health Policy Committee, NASPE Health Policy Committee and the Executive Committee of NASPE.

DR. T. SIMMONS: I think Dr. Weintraub was sort of being the devil's advocate here and hoping that you would say something that maybe I will try and drag out of you.

Is this a benign device, is this going to hurt people?

DR. TRACY: I think there is the potential that it will hurt people. I think that a device that puts something uninterpretable in their hands is potentially life-threatening. Some things that may not be life-threatening to a patient with a structurally normal heart may be life-threatening to a patient with Reggie Lewis' type of cardiac condition.

I think that this can give undocumented or unsubstantiated or uninterpreted data to somebody who has no

power, no knowledge to deal with the information that they are given. It is not appropriate for Reggie Lewis to manage his own rhythm disturbance. It is not appropriate for a patient with hypertrophic cardiomyopathy to try to determine whether the seven beats of v-tach that were picked up is potentially life-threatening or not.

DR. SWAIN: I think as Tony was saying, what we are skirting around is the two issues that we always deal with, safety and efficacy, and I think that will engender a very interesting discussion here.

I think the drug people probably have far more experience than we do in over-the-counter type things. This is the first time in my seven years on this panel that this issue has come up, so it ought to be a fascinating discussion.

Are there any other questions for Mr. Morgan or Dr. Tracy from the panel members?

[No response.]

DR. SWAIN: Then, I would like to ask any other members of the audience -- this is part of the open public hearing -- if anybody else has comments about anything.

[No response.]

DR. SWAIN: So there is no further discussion. Then, we will start our open committee discussion of the Premarket Notification Application for K963904, the Heart Alert, Inc., Cardiac Event Recorder.

The first presentation will be from the company. I would remind the panel members that this large sheath of papers they got this morning, I think the last two-thirds are the slides from the company.

The company representative, introduce yourself and financial class.

Company Presentation

MR. COSTELLO: Good morning, ladies and gentlemen. My name is Paul Costello. I am the President and stockholder of Heart Alert.

Before we begin this morning's presentation, I would like to take any opportunity to introduce to you some other members of the organization.

John Hoggle, Chairman and Chief Executive Officer of Heart Alert. Our science adviser, Dr. Lowell Harmison. Wayne Moseley, Executive Vice President. And beginning this morning's presentation, Dr. David Brill, M.D., fellow of the American College of Cardiology.

Dr. Brill's training includes a medical degree from Columbia University, internships and residency at

Yale-New Haven, fellowships at Johns Hopkins and the National Heart, Lung, and Blood Institute, and 10 years of clinical experience, as well as a clinical professorship of medicine at Brown University.

Dr. Brill.

DR. BRILL: Thank you. Good morning, everybody. As Mr. Costello said, I am a stockholder in this company.

I would like to start out by saying that Heart Alert shares most of the same concerns that were just brought up by NASPE, and our first task was to address those concerns, so that we could feel comfortable with offering this kind of a service.

I will outline to you today what we hope to do, a little about Heart Alert's experience in this market, and hopefully convince you that by extending this service to subscribers we will be giving them a useful benefit.

[Slide.]

Again, just so the committee understands, I am a practicing cardiologist. That is my full-time job. I practice general cardiology in Providence, Rhode Island. I am an assistant clinical professor at Brown University Medical School, and I deal with patients with arrhythmias as part of my general practice.

[Slide.]

Our goal at Heart Alert is to somehow extend the benefits that we have all realized through the use event recording and arrhythmia monitoring to a broader population of people. We hope that we can reduce barriers to medical attention that already exist and empower the individuals to take some responsibility for their own health.

We hope that we can provide long-term support to subscribers who may have ongoing concerns and anxiety about their health by giving them some immediate feedback and assistance when necessary.

[Slide.]

As you all know, there are millions of people in the United States who suffer from symptoms that are suggestive of an arrhythmia, and as you also all know, it is often extremely difficult to make any diagnosis or give any reassurance to these people because they are never in your office when they have the symptom.

[Slide.]

The National Ambulatory Medical Care Survey in 1991 looked at 12 million visits for symptoms of arrhythmia. There were 3 million people complaining of palpitations and abnormal pulsations, 1 million complaining of fainting, and 8 million complaining of vertigo.

[Slide.]

In this population, there were 13,000 episodes of pre-excitation syndrome diagnosed, 20,000 episodes of AV nodal re-entry and tachyarrhythmia, 25,000 episodes of atrial tachycardia or flutter, and 150,000 episodes of ventricular tachycardia.

[Slide.]

Now, as you all know, initially, the electrocardiogram was the only useful way we had to document any arrhythmias, and it required that the patient be in the physician's office at the time they were having the symptom, which was obviously not very practical.

Holter monitoring then allowed us to record the heart rhythm for 24 hours at a time, and more often than not, again, the symptom did not occur during that 24-hour period.

[Slide.]

When event report recording became widely available in the 1980s, we were able to monitor patients for an extended period of time, 30 days, sometime 60 days, and our ability to actually pick up arrhythmias was vastly improved.

[Slide.]

In 1989, the American College of Cardiology and American Heart Association developed the guidelines for

ambulatory ECG recording.

[Slide.]

They described three classes and indications for use. Class I was conditions for which there is general agreement that an ambulatory ECG is a useful and reliable test. Class II were those conditions for which an ambulatory ECG is frequently used, but there is a divergence of opinion with respect to its utility.

When they looked at various disease entities and cardiologic problems, in general, they came up with these symptoms and these classifications. Class I included symptoms of palpitations, syncope, and dizziness, and Class II were symptoms of shortness of breath, chest pain, or fatigue.

[Slide.]

This is just one example of a paper describing the effectiveness of transtelephonic cardiac monitoring. As you can see, there were 63 reports of palpitations, 34 of dizziness, 16 of chest pain, 5 of dyspnea, and 6 of syncope. As you can also see, there were significant percentages of arrhythmias associated with those symptoms.

Of those patients complaining of palpitations, 70 percent had some arrhythmia identified. Of those complaining of dizziness, there were 32 percent who had

identifiable arrhythmias. Of those complaining of chest pain, there were 6 percent identifiable arrhythmias, and of those with dyspnea, 40 percent, and syncope, 33 percent.

[Slide.]

This slide outlines Heart Alert's own experience in November of 1996 with approximately 2,700 patient calls. There were 1,145 complaints of palpitations, 463 of chest pain, 518 of dyspnea, 354 of heart racing, 163 of fluttering, and 54 of fatigue.

As you can see in the far righthand column, there 70 percent of those patient with palpitations who had arrhythmias, 12 percent with chest pain, 51 percent with dyspnea, 37 percent with heart racing, 25 percent with fluttering, and 31 percent with fatigue.

[Slide.]

Now, as useful as this system is, and we all use it in our daily practice, there are some significant problems we feel. The first is a problem that there are barriers to access to the device. Patients often have some sense of denial and choose not to go to a physician for whatever reason. Communication between the physician, the monitoring service, and the patient is not always ideal.

The duration of monitoring as it is currently used is generally only 30 to 60 days and rarely can be extended

longer, and there is limited availability based on some patient's insurance plans or health care payers.

[Slide.]

Oftentimes people do not have a designated physician, and the question is can we help these people who have not seen a physician by identifying a significant problem. Another problem that we encounter is that a device is prescribed for a patient, but they don't feel they are getting adequate feedback from their physician, who may view a normal rhythm strip and simply won't take the time to call them back and say, oh, yes, that strip was normal.

Patients travel beyond their local area and are in immediate touch with their physician and don't know who to call or who to contact when they are far from home, and as I mentioned before, there may be administrative problems in terms of the patient's ability to get the device through their current health plans.

[Slide.]

Patients don't come to doctors for a lot of reasons. Some fear loss of control. There is some anxiety associated with visiting the doctor, and there is the inconvenience of making an appointment when the person may be working or have children to take care of.

[Slide.]

Communication can be a problem because of the inaccessibility of health care providers when they are busy with other patients or doing procedures, the response can often be inadequate. For those of you who cover for other physicians on the weekend will know that you may get a phone call from a patient who has symptoms of palpitations and you don't know the patient, you have no data on that patient, and chances are they don't have an event recorder to help you at that time.

Physicians are not always available, and if you deal with covering physicians, the consistency of the response to the patient is often variable.

[Slide.]

Arrhythmias are notoriously transient and 30 days and 60 days may not be enough time to pick up arrhythmias. In addition, many patients want continued assurance. I have many patients and whom I have said, you know, this really isn't a problem, we have seen it, we have done the event recorder, they are nothing but benign PVCs, and yet despite that reassurance from me, they are still worried.

Patients who have cardiac surgery or myocardial infarctions often get some sense of comfort from having a device available even if, from a purely medical perspective, the diagnostic yield may be relatively low.

[Slide.]

We feel that a subscriber-based service could alleviate many of these problems. It would provide improved acceptance, enhanced communication, the ability to monitor for an unlimited duration of time, and empowerment of the individual to take some more responsibility for their own health care.

[Slide.]

It is our intention to use the same monitoring service and the same devices which we currently use in our physician prescription service and apply these to the subscription-based population.

This would allow us to reach a broader population and simplify the access of more people to this valuable technology.

[Slide.]

Subscribers are given an 800 access number that is available 24 hours per day, 365 days per year. When they call this number, they get an immediate response and immediate advice from the person at the other end of the phone. There is instant access to subscriber data, which we will show you later, was collected at the time of enrollment.

[Slide.]

We believe this would improve acceptance and communication among subscribers. Subscribers would be the ones who initiate the service, control the service, and decide how long they want to use it.

We have set up systems which we believe simplify the use of the device, and we provide direct subscriber communications, which is something they cannot obtain at this time when they call a monitoring service. There is immediately analysis of their rhythm strip and feedback including timely access to emergency services when that is appropriate.

[Slide.]

Now, the question is who can benefit from this device and who can be hurt. The list that you will see before you was taken directly from our 510(k) and outlines a number of people who we think are especially at high risk for arrhythmias, are those people who would benefit from the reassurance of having such a device.

There are those individuals who want to maintain some control over their own health status, those individuals who experience palpitations, fatigue, fluttering, chest discomfort, shortness of breath and heart racing, those individuals with known coronary artery disease, or who have known risk factors for coronary artery disease.

[Slide.]

Those who have congenital cardiac anomalies, those who are in physiologic decline and may be suffering from some decrement in their cardiac performance, those who have acute and chronic periods of anxiety and depression, and those who take medications and/or stimulants that could produce alterations in cardiac rhythm.

[Slide.]

Finally, there are issues of location, those who travel beyond their local area on business or leisure and may have difficulty contacting medical personnel, those who do not live nearby to an emergency medical center or a health care provider, and those who are beginning or engaged in an exercise program.

[Slide.]

At this point what I would like to do is show a brief video, which is the video that would be given to a potential subscriber when they enroll in the program, and then Paul Costello will describe for you more about our operations at Heart Alert.

[Videotape shown.]

MR. COSTELLO: Before I begin, I would like to clear up just a brief oversight and introduce to the panel, Dr. Catherine Faust, Vice President of Operations of Heart

Alert. I apologize.

[Slide.]

Let me take an opportunity now to describe to you Heart Alert's personal heart device and subscriber-based monitoring service. The PHD is approved device K944362. At FDA's request, the case mold has been modified to seal the lead wire port and the labeling will reflect Heart Alert complete with the 800 number.

The subscriber-based monitoring service is identical to the current physician-based monitoring service. Heart Alert's monitoring technicians, who are certified, are available 24 hours a day, every day. These technicians are supervised by physicians.

[Slide.]

I would like to define for you now the procedure by which an individual would become a subscriber. I would like to point out that this procedure will include a full disclosure of all benefits, indications, contraindications, and that all questions with the individual will be answered prior to them enrolling and becoming a subscriber.

The first step would an individual would call our 800 number and speak with a Heart Alert subscriber representative. Heart Alert would provide the individual with details, indications, contraindications.

[Slide.]

Heart Alert would then complete over the telephone an enrollment form with the individual where we will extensive information. This will ensure that during this enrollment period, a full description of the monitor and the monitoring service has taken place, that it has been clearly detailed with the individual how their device works and how the service is used and how the subscribers and the monitoring service will work together.

[Slide.]

As part of this enrollment form, we will gather general and demographic information, physician information, emergency medical facility information, medical history, and a risk factor profile.

[Slide.]

Once an individual elects to become a subscribers of the Heart Alert subscriber monitoring program, they will receive the following package: a PHD device with batteries and carrying case; an instructional video, a portion of which you have just seen; a quick reference guide, as well as instruction manual outlining the use of the device.

One other very important critical piece of information they will receive in this package -- and I would like to take an opportunity to pass a copy to each one of

the panel members --

DR. SWAIN: Could I also ask if you happen to have the device -- excuse me, you are not allowed to give out anything that is not in the panel packet, I am sorry. My keeper has just informed me of that, I am sorry.

If you happen to have a prototype of the device, it is nice to pass down, and we can look at that while we go.

MR. COSTELLO: We were fortunate enough to make an overhead of this last piece of information.

DR. SWAIN: And you can give a piece of that information to our executive secretary, who can then decide what to do with it.

DR. STUHLMULLER: It is in the package.

DR. SWAIN: What you have in the presentation can't include anything that is not in the panel packet already.

It's in the packet. We have already got it.

MR. COSTELLO: So, you have it.

This last piece of information to be included in the subscriber package is the subscriber's designation and certification statement. This will be where this subscriber informs Heart Alert of where emergency information is to be sent and how Heart Alert will communicate with the

subscriber's designated either physician or medical facility.

Heart Alert will not activate any subscriber's enrollment until hardcopy of this designation form is received and entered into our records.

DR. BRINKER: What if the patient doesn't want to give a physician's name?

MR. COSTELLO: This designation states either a physician or a medical facility. They must designate someone.

[Slide.]

Once Heart Alert receives this information, we will schedule a subscriber orientation session. This is to be a telephone conversation designed to last several minutes, which will involve an extensive discussion between the subscriber and the Heart Alert technician.

The objectives during this orientation are to provide detailed demonstration and repeated device use on behalf of the subscriber, so that it will ensure that they are, one, comfortable with the service, and comfortable with how to operate the device.

During this period, as well, we will obtain a baseline ECG reference strip, which will be permanently stored in our database, and this orientation procedure will

be repeated whenever the subscriber feels necessary.

[Slide.]

Now, Dr. Brill will speak with you regard the medical protocols.

[Slide.]

DR. BRILL: Again, our concerns are the same as NASPE's in that we want to make sure that people get the proper attention for the proper symptom. As was pointed out earlier, most of the time patients transmit strips that do not require immediate attention, and they have symptoms that don't require immediate attention. There are however, certain sentinel rhythms and symptoms that we feel do require immediate attention.

There are symptoms, rhythms and symptoms that also require a callback from a Heart Alert technician.

[Slide.]

The symptoms we have defined are loss of consciousness, chest pain, severe abdominal pain or nausea, severe dyspnea, any throat, arm, and/or jaw pain, and persistent dizziness. If a subscriber calls up complaining of these things, they are referred immediately to the medical designee that they have given us, or if they are traveling out of state, we will contact the nearest medical facility for them.

[Slide.]

The following is a list of rhythms that we believe require immediate medical attention. It is slightly modified from what is in the 510(k) submission because we felt that we needed to be more conservative in our subscriber-based service than we are in our physician-based service.

Those patient with sinus tachycardia above 140 beats per minute.

DR. SWAIN: Excuse me. This falls into the same category of new data that is not in the PMA, and I think your heart rate thing, as I recall, was 180 to 200, and there are other things.

John, do you have any suggestion on how we handle this?

[Pause.]

Good. it's my discretion. I think we will do this, but with the acknowledgment of the panel that this is really totally different from what we all read. Dan?

DR. SPYKER: It would certainly be useful to us if the speaker would identify the changes from what they have given us in the panel packet. That will be useful.

DR. BRILL: Certainly.

DR. SWAIN: What it was and what it is now.

DR. BRILL: Initially, sinus tachycardia was 180 to 200 beats per minute. It is now 140 beats per minute. Sinus bradycardia below 50 beats per minute with symptoms --

DR. SWAIN: It was 40, wasn't it?

DR. BRILL: Page No. 18. Again, I apologize, but because we share the same concerns that NASPE does, we wanted to make sure that, if anything, we erred on the side of sending patients for medical help rather than reassuring them when they shouldn't be reassured.

Sinus bradycardia previously as symptomatic rates less than 40. We have now defined two subsets, symptomatic, less than 50, or asymptomatic, less than 40.

Wide complex tachycardia was previously defined as sustained, which as you know is open to interpretation. We have now defined that as eight beats or greater.

[Slide.]

Atrial fibrillation and flutter of new onset or with rapid ventricular response remains unchanged. There is actually a typographical error on this slide. Premature ventricular contractions that are multifocal and symptomatic, pauses of greater than two seconds with symptoms or greater than three seconds without symptoms. Previously, it was simply pauses of greater than three seconds.

DR. SWAIN: Let me tell the panel members that can't find it, it happens to be on the supplement that we didn't get with our original book, page 18.

DR. BRINKER: No, it's in the main packet, page 18.

DR. SWAIN: Except the main packet doesn't have page 18.

DR. SPYKER: If you put it in your main package as you were instructed, then, it will be in your main package.

[Slide.]

DR. BRILL: Acute onset of second-degree or third-degree heart block and sustained supraventricular arrhythmias.

[Slide.]

In addition, any transient symptom without logical explanation would warrant a callback.

[Slide.]

DR. SWAIN: That's an addition, correct?

[Slide.]

DR. BRILL: Yes. What I would like to do is go over the protocols that are currently in use at Heart Alert, as well as the subscriber service, and it is obvious to you that they are precisely the same.

When a subscribers calls Heart Alert, the

technician identifies the person, their location, their identification number, and a phone number where they can be reached.

[Slide.]

The technician then goes over the sentinel symptom list to decide if that subscriber is in need of immediate medical attention. If it has been determined that they do not require immediate medical attention, then, they will be instructed to transmit the ECG over the telephone as previously described.

If the patient is sent for immediate medical attention, that information is not lost. The PHD contains the rhythm strip and can be interrogated later after the patient has arrived at a medical facility.

If there are significant ECG abnormalities according to the protocol, then, that patient would also be instructed to seek immediate medical attention. In the event that the patient could not contact a medical person by themselves, Heart Alert would do that for them.

[Slide.]

Now, the most important thing is our quality assurance. Each technician is observed weekly through five encounters with a subscriber. Ten percent of all ECGs are overread by a supervisor and one percent of all ECGs will be

overread by a cardiologist. In addition, all encounters that result in referral to a health care provider will also be reviewed by a Heart Alert cardiologist.

DR. SWAIN: Is this in our packet?

DR. BRILL: I am sorry, no.

DR. SWAIN: I am having kind of a hard time because I can't remember reading this stuff.

DR. BRILL: I apologize. We anticipated that the panel would have a lot of questions about quality control, and these were not in the initial 510(k) submission. We can leave them out and use them as answers to questions if you prefer.

DR. SWAIN: No, no. I think I made a decision we wish this. I just wish we had it before.

DR. BRILL: I apologize.

[Slide.]

This is an example of the subscriber call record. Each time a subscriber calls Heart Alert, there is a permanent paper record of that interaction, which obviously includes the patient's demographics, as well as their symptoms, any additional comments, whether or not an ECG was transmitted, and the quality of that ECG, the analysis of the rhythm, identification of the technician who handled the call, and the actions taken at that time. Again, this is a

permanent part of the subscriber's record. This, too is not in your packet.

[Slide.]

One of NASPE's questions was who is Heart Alert and who is going to be at the other end of the telephone. Heart Alert has been in the arrhythmia monitoring field for approximately 10 years. In 1996 alone, Heart Alert handled approximately 30,000 patient calls up to December 1st, 1996, and there were so significant complaints by patients, physicians, or medical staff.

Of these calls, a total of 3,600, or 12 percent, required medical intervention by a physician, and 1 percent required emergency medical care.

[Slide.]

In the third quarter of 1996, Heart Alert handled approximately 6,825 calls. Seventy-six percent of these patients had documented symptoms related to their primary diagnosis, and 48 percent of these symptoms were correlated with significant findings of dysrhythmia. Excuse the spelling.

[Slide.]

What I would like to emphasize once more is that it is Heart Alert's intention to take the same system that has been proven to be effective in the prescription-based

market and apply that to a subscriber-based market. We think we have proven technology and proven experience in the field, and that the benefits of arrhythmia monitoring can now be extended to a larger group of people.

Thank you.

DR. SWAIN: Thank you. The data you just gave on your proven system, we also, as far as I know, from my reading don't have that in the packet either, correct? Some of it, but a lot of it is not in the percentages.

Is that the conclusion of the company's presentation?

DR. BRILL: Yes.

DR. SWAIN: Thank you very much.

Our next presentation will be from Carole Carey, the FDA reviewer on this.

I guess I need to ask you, you know, normally, we receive the FDA reviewer's review at least several days ahead of time, which I think we only have a couple page thing here. Do we have a reason for that on this one?

MS. CAREY: That is all I have. It is very short.

DR. SWAIN: We are required to have a break at certain times, and this appears to be the time. So, we will go on a 15-minute break and we will be back here exactly at 10:45 to continue.

[Recess.]

DR. SWAIN: The next presentation is by Carole Carey, the FDA representative.

DR. SPYKER: My name is Dan Spyker. I will close out the FDA presentation.

FDA Reviewers

MS. CAREY: Good morning. My name is Carole Carey and I am a scientific reviewer for the division.

[Slide.]

Cardiac event recorders that transmit electrocardiograms over telephone lines have been classified by the Cardiovascular Devices Panel as Class II prescription devices. They are identified in the Code of Federal Regulations as CFR 870.2920.

The patient activated cardiac event recorders intended for ECG monitoring have also established experience in electrode technology and transtelephonic ECG data transmission in ambulatory patients.

[Slide.]

Today, Heart Alert, Inc., of Douglasville, Georgia, is seeking the introduction into U.S. interstate commerce a device known as the Personal Heart Device, PHD Cardiac Event Recorder. In conjunction with the Heart Alert Cardiac Monitoring Service, Heart Alert, Inc., requests that

the PHD monitor be made available as an over-the-counter, non-prescription medical device.

The sponsor is not requesting that the PHD monitor be sold as an "off-the-shelf" item available through supermarkets or pharmacies like over-the-counter test kits, blood pressure apparatus and others, but instead, patients will obtain the device, training, and educational information about the Heart Alert monitoring program and service through telephone interaction with the prospective subscriber. Heart Alert filed a premarket notification application to exclude the non-prescription labeling on September 30, 1996.

For the record, one of Heart Alert's slides previously stated that the PHD is approved by FDA, and it has not been approved by FDA.

[Slide.]

The PHD Heart Alert System consists of the following: the PHD ECG recorder/transmitter, which is identical in form, circuitry, specifications and functionality to the commercially available HeartCard Cardiac Event Recorder manufactured by Instromedix. FDA granted the market clearance on September 7, 1995 under K944362.

Both credit card-sized, 1/4-inch thick PHD and

HeartCard monitors acquire the ECG signal from the skin surface of the chest using metal electrodes that are capable of recording three, 30-second events.

The events are stored in solid state memory and sent for later transmission via telephone lines to the ECG receiver at the Heart Alert Cardiac Monitoring Service. Heart Alert uses a commercially available PC-based patient testing system which processes the incoming signal to be displayed on screen or print a hard copy. The computer software was developed by PaceArt, Inc., and cleared for intended use on April 14, 1992, under K915632.

[Slide.]

The PHD monitor is virtually identical to the predicate device and has undergone safety and effectiveness review by FDA. Therefore, from both the technical and clinical standpoints, the safety and effectiveness evaluation of the PHD Heart Alert System focused on issues related to the device's new intended application, that is, a non-prescription device.

I will briefly discuss the engineering assessments. Dr. Spyker will present the labeling issues for today's discussion with the panel.

First, we suggested design requirements and assessed any potential risks to the patient. We specified

that the device must be simple, easy to use, and pose no safety hazard to the self-identified subscribing patient.

[Slide.]

In the proposed Heart Alert System, that is, without a prescription, the potential users must rely more on the interaction between themselves and the Heart Alert staff who is in a remote location, in addition to the user directions and video instructional materials. Typically, patients may have the added benefit of an actual demonstration and direct personal instructions from the prescribing health care practitioner or his or her designated staff prior to using the device in the real environment.

We were also concerned with the external electrode lead port. The port is an access interface to electrically connect a wristband type electrode cable. To simplify the use of the PHD monitor and reduce any potential electrical shock hazards, the PHD device was modified to physically block the external lead connector.

This will prevent an individual subscriber from inserting other types of cables or objects into this connector. The plastic mold casing now has a continuous, closed side where the leadset "door" formerly was. The original equipment manufacturer, Instromedix, will continue

to manufacture the PHD device for Heart Alert, Inc.

[Slide.]

We also asked Heart Alert, Inc., to evaluate the PHD monitor for signal changes and data quality based on subscriber use and misuse related to improper placement of the recorder on the chest. Five different orientations from the normal proper position were analyzed.

The various positions included 90 degrees, 180 degrees, shift left, shift right and an obscure tilt position relative to normal position. Examples of the resulting ECG rhythm strips and Heart Alert's recommended approaches are on pages 24 to 29 of the supplementary panel package.

Thank you.

DR. SPYKER: My name is Dan Spyker. I am the Deputy Director for DCRND.

[Slide.]

What we need from the panel today is really pretty simple. We would like you to discuss the benefits and risks of the prescription/non-prescription use of this device and we would like you to provide your recommendations at the end of the day.

[Slide.]

This fundamentally becomes an issue of can we

label properly such that it will permit the patient to determine whether the device is appropriate for them, provide adequate directions for use, so the patient can carry out the acquisition and transmission rhythm strip, and this, as Carole has described very well, has been covered, and as you heard some data of experience of the company, is up and running today in terms of the monitoring service that we expect to use, so not any substantial change here.

The third thing of course will be to provide appropriate triage for treatment based on the information gathered through use of this device.

Now, this is subtly different from what the existing system or the prescription system, as you have seen, and one of our panel members asked, what if the patient decides that he doesn't need a doctor.

The way it is currently proposed is either a physician or an emergency facility, so some sort of designation. So that is subtly different. So, the doctor may not know when they are going to get -- if it is your patient, you may or may not know your patient has participated.

[Slide.]

Now, the agency has focused on consumer labeling. This document, which has been passed out to the panel

members, called "Write it Right," and if there is any sponsors in the audience or anyone who is interested and hasn't got a copy of this, then, you need to leave here with one today. Do not pass go without your copy of Write it Right.

The fundamental goal of that document guidance is to create understandable instructions for home health care device users. It deals with the planning, the format, content, writing, and testing of user labeling or user instructions.

At the back of your handout that came to each of the panel members today, the first part of that, I am basically going through that memo. All the overheads are directly from that memo, if you will. The last part of that memo, like page 7 and 8, is a copy of the summary check list from Write it Right, and that gives you a very good flavor for what the document suggests.

Format and content are some 27 points in that check list, including the like 3 through 19 of that check list are the sections that we expect to see in consumer labeling, and a number of 8 or so of the check list refer, if you will, to the process, in other words, figuring out what you are going to do in developing and actually testing.

[Slide.]

Now, when I use the term "labeling," label, as you probably know, refers to what is on the outside of the package, so we might think of how the consumer is going to access this. It might be from an ad, it might be from a print ad or a media ad. So, we certainly want to include that as part of labeling. Label is the outside container, what is printed on the outside of the container or, for example, what is on the little card certainly would be a label.

Labeling, in this particular case we are taking a fairly broad perspective, and we mean the advertisements, promotional materials for the devices and the service. We mean the patient registration process including the forms, which have been shown and are in your pack, the patient instructions, printed, video, telephone, training, and we mean the monitoring service function including the triage and follow-up protocol. So, I consider this all to be in your purview in the category of labeling for the purposes of our discussions today.

[Slide.]

Now, this is sort of a chicken and egg problem. You say, well, can we develop labeling is your fundamental question, can we label this for non-prescription use, but I am suggesting that let's give it our best shot at developing

labeling first, okay. So, I don't want you to ask the question is this possible or not at first. I want you to assume it is possible first.

So, what I am going to take you through is some examples or some suggestions, and I want you to focus on the indications and contraindications, and keep in mind, as I suggested, there may be various uses for these wordings. It may be part of -- if it is going to be an ad in the Ladies Home Journal, we want it to be even-handed. We want it not give all the benefits and none of the risks.

So, it may be that part of the patient instructions almost certainly would find its way into that, but it may be part of advertising, as well. Keep in mind we are writing this for the patients, we are not writing it -- the usual ruminations that we go through in this panel are writing prescription labeling.

We are talking about doing it for the patients now, so you will see, particularly in the examples I am going to show you, we have really kind of toned down -- we are shooting for sixth through seventh grade level is what we are shooting for when we finish this document.

[Slide.]

I have intentionally put some real fine print because this is already in your panel pack, and this is the

only indications that were included were this version.

[Slide.]

There are basically 10 point. For example, this says individuals who have acute or chronic periods of anxiety or depression. Now, our initial impression was this might be a little broad, so the second version -- well, this next slide is the contraindications that go along with this.

[Slide.]

It says who should not use it. This is a contraindication in our view. If you have any disability that would prevent you from placing it on your chest, your bare chest, and operating a telephone, that is the only contraindication in the version that we put in the panel pack.

[Slide.]

The B version, these are now in the memo that was passed out to you this morning. The B version, we focused it down somewhat. This the whole of the indication section, the whole of contraindication section. I am going to read through these, so we have them in the record, I guess.

So, for our indications, first, our suggestion you start with the disclaimer. Simply you can have a sensation of an irregular heart rhythm without having serious heart problems, and you can have a serious rhythm problem without

any sensation.

The next paragraph says you might benefit from using the PHD and the HA monitoring service if you have heart problems related to an irregular heart rhythm and/or your doctor want to be able to test your heart rhythm while you are experiencing symptoms. This device can record your heart rhythm for periods of 30 seconds.

The last paragraph here says arrhythmias are more likely to occur if you have heart failure, coronary artery disease, history of arrhythmias, and/or valvular heart disease. The device and service may be most useful for you if you are having heart rhythm problems.

The monitoring network offers rapid referral to appropriate medical facilities and provides these facilities with your rhythm information and the medical history you have provided. That is the registration form that we went through and is in your panel pack.

What we have suggested for contraindications, the first is similar to the one in the previous contraindication you have got to be able to put it on your chest, and the second one is one that we have been working on, and both the B and C version have been a joint effort with the sponsor and the review team.

So, if you like them, I did them; if you don't

like them, that is fine.

This device is not a substitute for medical attention. It is a diagnostic device which, when used in conjunction with the Heart Alert monitoring service, can provide useful -- this should say useful diagnostic information regarding your heart rhythm. This device is for monitoring purposes only and has no therapeutic value.

[Slide.]

The last one is a three-bulletized version of the previous one, if you will, so it is basically the same. Who should use this PHD - persons who experience symptoms suggestive or abnormal rhythm including -- and we have got these nine bullets.

Who should not use it, and we have got history of arrhythmias -- well, what we have suggested here is some prose that I think might be reasonably useful. It says you should not use it without consulting your physician.

Now, if there are situations -- I think the last article in your panel pack from Mayo, the study that was reported in there, they specifically excluded from that study of the event monitoring anyone who had what they considered a dangerous arrhythmia, a potentially lethal arrhythmia.

So, I think one of our real challenges, as you

will see when we phrase the questions, is can we exclude these people, should we be excluding these patients, and how we could we do that in the labeling.

Now, I will point out to you that we have got history of arrhythmia here in both indications and contraindications, which might confuse you if you weren't really insightful about this process, but it is easier to cross them out if you decide when we are working on this draft that you want to take it out of here, but it might show up either place.

DR. GREGORATOS: Dr. Spyker, I want to understand correctly. Version B and C are your versions, the agency's versions?

DR. SPYKER: No, they were developed jointly with the sponsor. Version A is what went out in the panel pack. B and C, I think are trying to get us closer to something that -- we are trying to give you some suggestions for what you might wind up with. We don't want to pretend, because we haven't yet decided what the indications and contraindications ought to be -- but we want to give you some stuff to work with, we think a little closer to the final product that the Version A was, so the sponsors worked with us on the B and C version.

So, we have got two classes of questions. Based

on the data presented, Question 1 is how would you describe the patient population for whom the use of the PHD-HA system -- and the emphasis here is on the whole monitoring, as well as the detection system -- would be safe and effective without the order of the health care professional.

Likewise, No. 2 is how would you describe the patient population for whom the use of this system would not be safe and effective without the order of a health care professional.

Then, of course, what is the appropriate indications, which I am proposing we might work on first, and contraindications for these populations. And if we get that far along, have gotten a thumbs-up on some population, Question 4 is are there any further modifications to this system, patient follow-up, and use of the PHD system that you would recommend.

[Slide.]

The last slide, if you all or any of you believe there is no population which we can safely do this in, then, you need to answer the question where should we begin. I think this is really not a matter of if we are going to have this kind of technology eventually available, but when, and I don't know whether it is now or later, but if it is going to be later, if this is not making the grade at this point,

we need to give some thought to where to begin.

That is all I have.

DR. SWAIN: Let me just ask you one question. You are talking about the PHD system, and I want to make sure that we are considering for especially safety and maybe efficacy, that a device is not just metal and plastic, but it includes the data and, in this case, the data monitoring subscriber system, so, in fact, you meant system, not single device.

DR. SPYKER: Thank you. That is what I meant.

DR. SWAIN: We are going to go around our usual way and have our primary reviewer, Dr. Curtis, to ask questions of either the company or the FDA on this. We will have 15 minutes for the primary reviewer of questions and then 10 minutes for each panel member, and we will keep going around until everybody has all of their questions answerer.

Dr. Curtis.

Panel Reviewer

DR. CURTIS: Thank you.

As has been stated previously by Dr. Tracy, event monitors are appropriate for the documentation of cardiac arrhythmias that may be responsible for symptoms such as palpitations or dizziness.

I use event monitors all the time in my own practice, cardiologists do in general, electrophysiologists use a ton of them, and we use them in order to document the suspected cardiac arrhythmia or sometimes, almost more important, is to document that there is no arrhythmia when a patient has some specific complaints, so they are very, very useful.

I think one of the key points here is that I don't give out an event monitor to everybody who shows up in my clinic, and I strongly doubt anybody else does either. Well, why is that? The answer to that comes into the safety and efficacy questions.

First of all, why wouldn't I give out an event monitor to everybody? Well, sometimes it is inappropriate for what a patient is complaining about.

One of my jobs as physician and why we went through all the training that we did is to get a patient's complaints in, to analyze their history, to do a physical examination, and then make an educated guess or a differential diagnosis as to what you think is going on, and then you prescribe the test that will help you get the right information.

Sometimes when a patient comes in and complains of dizziness or near syncope, we think it is vasovagal syncope,

and may wind up doing a tilt table and would never dream about using an event monitor. So, there are very specific indications for using these devices - predominantly palpitations or complaints of racing heartbeat, arrhythmias, and then some cases of dizziness or near fainting, that sort of thing.

I don't think I have ever given out an event monitor for a complaint of chest pain, and the reason for that is that if I gave it out, it would normally be because someone complained of a racing heartbeat or something that made me think there was an arrhythmia, but usually if somebody complains of chest pain, we have a different set of tests that we go through, treadmill tests, thallium sometimes, even catheterizations, all of which don't involve an event monitor.

So, when we get into the how could this lack safety for a patient, I think there are some very specific places where it could be dangerous for a patient to use this without a physician's advice, and one of those reasons would be chest pain.

In the labeling that was originally proposed, the A indications, and even getting down into B and C, if I remember right, there are indications, such as coronary artery disease risk factors or history of chest pain, I

think that is where we don't want to get into using this sort of thing.

I think the problem is that these are lay people, and I think what could happen with a device such as this is you get a patient who wants to check if their heart is okay, and then they go and use this monitor, and they get a recording, and they transmit it to the company, and they are told that there is no arrhythmia. Well, then, my heart is okay.

Well, that is not necessarily true. A patient could be having unstable angina, and I don't know of any data that says that an event monitor is an appropriate way to pick up ischemia as an etiology of chest pain.

So, in that case, we could delay getting appropriate medical therapy for a patient, even to the point of a patient risking a myocardial infarction or worse, because they are inappropriately using a device or picking the wrong diagnostic test for what they need.

There are other times when it is simply irrelevant to a patient's symptoms. You want to use a device that is efficacious for what a patient is complaining of. Patients could use these devices because they are just worried about things, and possibly in some cases, the worst thing is that a patient is going to wind up wasting a lot of their money

when it is totally irrelevant to whatever they are complaining about.

But I think if we want to market this thing, and kind of give it our seal of approval, then, patients should have some expectation that there is going to be value that they get out of it.

I think one of the factors in some of the data that was presented by the company, whenever there have been publications about event monitors and showing what percentage of the time we pick up an arrhythmia when there is palpitations or when there is faintness or all these different diagnoses, that is a best case scenario, and that is because event monitors are given for patients who have been prescreened by a physician as to some likelihood that there is going to be an arrhythmia involved.

If you take the general population and they use this for whatever complaint they have, those numbers would have to be lower, I don't know how low, but they would have to be lower. Specifically, in the case of chest pain, even then with a prescreened population, only 12 percent of the time did any kind of an arrhythmia get picked up, so that is one place I think where we would want to have that out.

There was an allusion before by the NASPE group about interpretation of arrhythmias. I think that is very,

very important. I don't know what a patient who has no medical background at all is going to think when they are told that they are having PVCs.

If you mention that to people, they usually don't know what that means. I think most people would panic, my God, I have got something wrong with my heart. It really is very context-specific. We may worry more about PVCs in a patient who has got structural heart disease, and a patient who has no structural heart disease, if I give them an event monitor for palpitations, I usually assure them ahead of time that I don't think they have got a dangerous problem, but we want to see exactly what it is and then analyze whether or not we want to do anything about it.

So, patients won't have a context with that, that I am a little bit concerned about.

There are times when, not only with chest pain, but other symptoms that an event monitor could be totally inappropriate. I recently had a patient who came to see me in my clinic for near syncope. Well, that is a good reason to use an event monitor in a lot of cases.

This particular patient, who had not been evaluated by anybody previously, when we examined the patient, obviously had aortic stenosis, and the appropriate therapy for that or evaluation for that patient turned out

to be cardiac catheterization and valve replacement, had nothing do with an event monitor.

In a situation like that, which I will admit doesn't happen every day, a patient could delay getting appropriate medical therapy to their detriment, so that is something I think that is important to think about.

The problem here is that some arrhythmias are life-threatening situations, many of them are not very important at all. Clues that a patient may have an arrhythmia could be vague, as well. I think some of those things have to be considered when we think about who would wind up using the device.

In terms of the original indications that were listed, it apparently is turning out now that those are being modified, and we have got these B and C versions, but I wanted to make a few comments about that.

I think intermittent symptoms, such as palpitations, racing heartbeat, that sort of thing, very appropriate to think about as a possible labeling indication for an over-the-counter use.

I would strongly argue that chest pain is not an appropriate indication, that risk factors for coronary artery disease are not appropriate indications, that anxiety and depression are not appropriate indications for an event

monitor. Mostly, that is just a waste of time and effort.

It wasn't until I got through some of the readings at the back of the packet that I believe the implication with the anxiety and the depression, if you look at the articles that were included in the packet that we got, is that there is an association between ischemic heart disease or structural heart disease and anxiety and depression, and if I read between the lines, it sounds to me that if you have anxiety and depression and, therefore, may have more of a risk of heart disease, therefore, you should use an event monitor to pick up some, that is a real stretch to me to get from point A to point D there.

So, I would really strongly argue about some of those, and even in patients who have medications and need to be monitored, I think a physician most of the time could advise a patient as to whether or not something like that is indicated.

So, I think a lot of my concerns, it is not just, you know, let's keep it to ourselves and not let patients have this therapy, I think it really gets into interpretation. I mean we don't allow anybody who feels like getting a CT scan for headaches get one. Why? Because most of the time you don't need it and it is just a waste.

And in here, when you are getting into the heart,

there are times when arrhythmias could be life-threatening. If I had a patient come to me who had structural heart disease and syncope, previous myocardial infarctions and syncope, I am unlikely to give them a event monitor and say go ahead and transmit this for me, let me see what happens, because the next event could be fatal, and I might handle that very differently from a 21-year-old who is having near fainting spells or a 45-year-old who is having near fainting spells.

In terms of some other specific comments -- let me just look through this -- I was concerned in the proposed subscriber enrollment form, which is page 22 in our packet, that there is no information on why the patient wants to use it, and I think that that is something that is going to be very important.

I don't think we want to label this for whoever feels like seeing what is going on with their heart try to use it, again, because most of the time that is going to be simply a waste.

Another factor, in the subscriber protocol for enrollment, on page 12, they talk about getting information on the patient's physical and medical history. I am sure all of us have had plenty of experience with patients who come in with complaints and really don't have a clue as to

what their medical history is or a very rudimentary understanding of it, and frequently we have to go through a patient's medical records to get a fairly good understanding of what is going on.

If we have to slant this at a sixth and seventh grade level, in terms of the labeling, to then think that that patient, who can only understand at a sixth or seventh grade level, has the understanding to transmit what is important about their medical history, they don't gibe, they don't go together.

I think that rather than this business about empowering patients and patients who don't have access to medical care, you could look at the flip side in that patients could use the device and delay getting appropriate medical advice rather than the other way around, where we say that patients can't get access to medical care and therefore they will use this.

In my own mind, all or almost all of the indications that were placed in A are inappropriate or need to be modified if we are going to have this as an over-the-counter use.

The final comment I want to make right now. We talk about empowerment, patients want feedback, they want communication. Now, I use a physician-prescribed services,

all of us do now, and I am sure yours is currently physician-subscribed, and this is a question I want to ask the company.

When you have a patient call in now, and they are having an arrhythmia, what sort of information do you give them. Maybe I am naive about this, but I can't imagine that the answer to the patient is we have got your arrhythmia, but we are not telling you anything, you are going to have to call your doctor to find out.

I mean there must be some sort of feedback you give a patient now, and how much different is that feedback going to be with an over-the-counter system compared to the physician-prescribed system that is going to be so much better that a patient gets benefit from that.

DR. SWAIN: One of the company members could answer, and then state your name for the audio record.

DR. BRILL: Dr. Brill. You raised a lot of points. Do you want me just to address your last one or to go through and --

DR. CURTIS: I want you to just answer the last question.

DR. BRILL: The difference in what we would do in the subscriber-based system is, yes, there would be some explanation to the patient. If the patient calls up with a

headache, which they may well do if they have their own device, or with palpitations, and transmit a normal ECG, they would be told by the technician that there were no identifiable arrhythmias, and if it wasn't one of those symptoms that we already mentioned, they would probably be told that at this time there doesn't appear to be a problem, but if the symptoms persisted, they should see their physician.

It is not our goal to be the primary diagnoser of disease. You may mentioned -- well, I won't go on. Did that answer your question?

DR. CURTIS: So, essentially, then, what the patient would be told over the telephone is the same whether it is a physician-prescribed system or the over-the-counter, is that what you are saying?

DR. BRILL: I actually would like to defer to one of our directors to talk about the current technician protocols, but you are right, at the present time, patients aren't just told hang on, wait for your doctor. They are given a little information. I think we will be giving them a little bit more information and a little more reassurance, but not --

DR. CURTIS: I think it would be important for us to know what the difference is there.

DR. FAUST: My name is Cathy Faust. I am Director of Operations for our cardiac lab.

DR. SWAIN: And your financial interest?

DR. FAUST: I am just an employee.

Currently, when a patient calls in and they are symptomatic, we go through a protocol and get their symptoms, and if it does not meet their physician protocol, their notification protocol, then, we tell them at that time because each of our physicians establishes -- we have an overall protocol that we go by -- and if it does not meet that protocol that we need to notify them with, then, we explain to them that if your symptoms persist, we need you to make a follow-up transmission, and we will contact your physician.

We don't tell them that they are having PVCs, we just tell them that their rhythm does not meet protocol, that we need to contact their physician at this time, but if their symptoms persist, then, they need to make a follow-up strip and call us back.

DR. CURTIS: What are you planning on doing with the subscriber system?

DR. BRILL: I think in the subscriber system, we will have to give them a little more information, so that it won't be confusing, and it will be a description that will

be pretty much boilerplate, that says, well, you have PVCs, in general, these are not serious, and again, based on if you have -- it will be tailored to each patient depending on whether or not they have a history of cardiac disease or arrhythmias or anything else that is on their present form.

DR. CURTIS: But you haven't had that worked out yet then.

DR. BRILL: We don't have the boilerplates in the submission packet.

DR. SWAIN: As a non-electrophysiologist and cardiologist, let me just ask you about the subscriber systems, either Dr. Curtis or Dr. Brill.

If I have my patient go to your system, do I then tell you when to notify me and what to look for, each parameter, is that the protocol you are talking about?

DR. BRILL: There is a basic protocol that the company uses as a standard, and if you wish to alter that in any way as the prescribing physician, you can alter it.

DR. CURTIS: I don't have any further questions.

Open Committee Discussion

DR. SWAIN: Dr. Gilliam.

DR. GILLIAM: I have several concerns and many of them have been addressed, and I will skip those, but one of the things, we were talking about patient empowerment, and

at one point we were talking about health concerns of patients. I am trying to figure out exactly what health concerns we are alleviating here.

If we look for arrhythmias with event monitors, if it is a life-threatening arrhythmia, ventricular tachycardia, those are going to be people with a history of serious arrhythmias, and so I guess we exclude those.

If it is a patient who has syncope where they suddenly pass out or fainting, we should exclude those because obviously, if you pass out or faint, you can't activate this device.

So we are left with those people who have just simply flutters or perceived racing heart without syncope or loss of consciousness. And that is literally it. So, I guess I am asking those who are marketing from the company, what health concerns do you see yourself alleviating in the population?

DR. BRILL: Let me give you another example. You have a patient with significant cardiac disease who you have evaluated, treated, and monitored to your satisfaction, that patient remains concerned. I know you have told me, Doctor, that these are just benign PVCs, but I am telling you they are driving me nuts. I have patients like this, and you can deal with them on a monthly basis, and they will call you

and you say, you know, gee, Mr. Smith, we have been over this, it doesn't sound like it is anything different, I really don't think you have anything to worry about.

I have a lot of patients like that. I believe that patients like that, who have a monitoring device, while agreeably, the diagnostic yield may be quite low, I don't expect that you are going to uncover something you haven't already diagnosed, but will that patient feel more comforted knowing that, yes, in fact, this is the same thing that was already diagnosed, they are just the PVCs that Dr. Gilliam keeps telling me I have, I guess it is okay for right now.

DR. GILLIAM: But in that case, if you have already made a diagnosis that they have just PVCs causing their symptoms, so, in effect, that patient doesn't really need this unless you have data that shows that carrying an event monitor carries with it some benefit.

DR. BRILL: The benefit is that the patient feels reassured, because you don't really know that what he has next month were PVCs, you know pretty well from your workup that that is what --

DR. GILLIAM: You didn't submit data showing that a patient carrying an event monitor --

DR. BRILL: Feels reassured? No, we don't have data about patients feeling some reassurance.

DR. GILLIAM: So essentially it is conjecture that a patient, given an event monitor as opposed to being counseled by a physician, because what you are talking, I see every day, patients with PVCs. I mean what they need is education about that if that is truly what they have.

DR. BRILL: Currently, patients can go out and buy blood pressure monitors. You treat patients with hypertension. I personally don't recommend that they check their blood pressure daily, even weekly. I have a lot of patients that do that. They may or may not present that blood pressure data to me. They feel reassured that they can keep track of their blood pressure and that they know that it is all right. I think there is precedent although perhaps not in arrhythmia detection.

DR. GILLIAM: I think the two subjects are somewhat different. I don't again tell the patients my drug closet is open, go ahead and treat yourself for hypertension, which may be potentially more along this line because in this situation, we are making as assumption that a patient has a significant arrhythmia when they may not.

But let's agree to disagree there. Looking at, you had a number of cases where you mentioned myocardial infarction, and, you know, heart attack and chest pain, I don't see any use for this in that, and I think it may give

patients a sense of false confidence.

They are carrying this HeartCard that is going to say their heart is okay. I think that is the biggest concern I have is the inability for us to adequately convey to the patient the difference between an arrhythmia and chest pain, looking at your numbers, and in the sheet that you handed out and your slides, and you had your experience --

DR. BRILL: We have no disagreement about chest pain. I personally, as you know, we are not allowed or we are not supposed to present revisions of the original document, I was not involved in the preparation of the original document. This is not a device to diagnose chest pain. So there is no disagreement.

I also agree that in our labeling, we have to be clear that this is not a device to diagnose an acute myocardial infarction.

DR. GILLIAM: But I think I would submit to you that we are going to be totally unsuccessful in doing that because even in your physician-prescribed group, a vast majority of your calls were those of chest pain, which everyone would agree it seems that chest pain is not an indication to call a transmission for an arrhythmia monitor.

DR. BRILL: Oh, absolutely agreed. The question

is if we exclude the entire population of patients with coronary artery disease, most of us in this room are probably excluded whether we know it or not, but I am not sure that you actually are providing them with any protection. It should be clear that it is not to diagnose coronary artery disease, but because you have coronary artery disease doesn't mean that arrhythmias may not be detected.

DR. GILLIAM: And to that line, you said you are not a primary diagnoser of disease as the service, but, yes, I think this is. I mean it is not there to diagnose what you already know. I presume that this is there to diagnose some new entity.

DR. BRILL: I think it is twofold, you are right. It is there -- we will make some diagnoses that were not previously suspected, either because patients have not been in contact with the physician or because an arrhythmia was detected that hadn't been expected.

Most of what we will do, as you know from your own practices, is receive strips that are of minor clinical consequence, and so a lot of what we will do -- which I realize you and I disagree about the benefit of the reassurance -- but that is a lot of what we will be doing.

DR. GILLIAM: How do you propose those patients

that you have sent to the emergency room, for instance, for the wide complex arrhythmia that has terminated, if you tell the patient to go to the emergency room, their insurance probably, in retrospect, may deny a great number of these payments. As a company, do you defer any responsibility or working with HMOs to that effect?

DR. BRILL: No, as a practicing physician, I run into this all the time. The patient goes to the emergency room with chest pain, it turns out to be esophagitis, and you may have an argument with the insurance company saying, how is the patient supposed to know that it was esophagitis before they were evaluated.

I think we stand on good grounds if we say this patient had an AP run of ventricular tachycardia, they deserved evaluation, but can we assure you that every HMO in the country is going to go along with that, we cannot.

DR. GILLIAM: Lastly, I think in your documentation, a lot of times you state ECG, I mean as opposed to a rhythm strip. This unit does not acquire an electrocardiogram. The use of electrocardiogram, you know, is confusing to physicians, and I think certainly would be implied confusion to patients. I think a good education program would be necessary to educate people that you are not obtaining an electrocardiogram.

DR. BRILL: Perhaps a single-lead ECG would be more appropriate terminology.

DR. GILLIAM: The last thing I want to do is I think there are several things, but I want to give other people time to look at this. Once statement says a technician is going to advise the most -- and then you said best course of action, so essentially, a person is going to receive a transmission, and a technician is going to make a decision and advise them their best course of action.

DR. BRILL: Right now in the prescription-based system, if you send a patient a monitor -- and, by the way, about 35 percent of Heart Alert's calls do send the monitor directly to the patient at the physician's request in terms of getting them enrolled and learning how to use it -- what happens is when they do a transmission, you do rely on the technician to know if they had a bad rhythm, because you are not there to receive it, and you do rely on that technician to tell you and decide if the patient is having some symptom that requires immediate attention, and these are the same technicians who you are currently relying on to make that judgment.

The difference is that rather than calling you and your service, they are going to send it to whomever the patient designated.

DR. GILLIAM: If there is no connection from a physician as far as designated, I mean when --

DR. BRILL: There has to be. They have to give us -- or an emergency room, and chances are -- I hope you are not on call every night -- but sometimes this call is going to go to somebody who has no knowledge of the patient, very similar to an emergency room, and the advantage here is when they get to the emergency room, we have something to give them, they are not just receiving the patient who was complaining of palpitations 20 minutes ago who they never met, they also get a strip that says this is what was happening.

DR. GILLIAM: The last thing is in your -- and this is looking at your video -- your video does not demonstrate the equipment you use as far as PaceArt. That was an Instromedix receiving station, not a PaceArt receiving station.

DR. BRILL: That's right.

DR. GILLIAM: So that technically is not the same.

DR. BRILL: That is correct.

DR. SWAIN: Dr. Brinker.

DR. BRINKER: Thank you. One of the problems we have I think is that we are not, for the first time, we are not asked to evaluate a device, we are asked to evaluate a

practice of medicine.

I know I use that term loosely perhaps, but in reality, that is what it is. I think there a couple of questions that I have that might, for instance, point to the difference between blood pressure cuff and this service that you are offering.

The patient buys a blood pressure cuff, and they get a reading which they interpret themselves. There is no implied censoring of that interpretation, whether they do it correctly or not, that is their empowerment, and then theoretically, if you had a device that they put on your chest that would automatically say this is what you have detected, that would be one thing, but now we have another thing, and that is that there is a transmission of this data, and there is an interpretation by a second party.

As you said before, the second party people are skilled in doing this, but it is still now they not only read it, but they make some sort of disposition to the patient or helps the patient make a disposition.

I guess I am a bit concerned about that. Let me get to a couple of specifics. Again, on Part B5 subscriber's designation, it basically says after leaving a space for the physician or medical facility's name, that if I do not designate a physician of record or presumably a

medical facility, that it is my sole responsibility to contact the medical facility or physician of record.

There is a disclaimer here --

DR. BRILL: I think there was a revision that was sent to the panel previously.

DR. BRINKER: This is the supplemental insert. You might look at your own copy because it showed pretty much the same thing that I couldn't read. I am concerned about that.

Also, I am concerned that this patient could put in Dr. Gregoratos, and Dr. Gregoratos could say I don't want to be legally at risk of being the guy that is to be notified if this person has a problem, because this suggests that there is some connection with the acceptance of that data by a physician or facility.

I think that the better way of doing this, and I know it is a way that you are not going to want to do it, but a better way of doing this is to have a physician sign off on this, and say that they are willing to -- this patient wants this -- they are willing to accept the information. They don't have to say whether they think it is a good or bad idea, but they accept the information and take responsibility for it.

I think that, as you said before, you have a good

service now, and what could be done to make it better. Quite frankly, I don't think that the way you have it configured is necessarily the way to make it better.

There are some issues that you suggest might be helpful to patients. One is that there are a certain number of patients that might have anxiety, they might do better with one of these. Then, the way to do this is to convince physicians that -- and physicians right now are very fixated on cost effectiveness -- convince physicians that this is a right thing to do for that particular patient.

I also would like to know, you say you sell a subscription to this basically to the patient. How long does that run? How does the patient enroll in this, a lifetime subscription?

DR. BRILL: If you are interested.

DR. BRINKER: But I mean it is important for me to know what the patient --

MR. COSTELLO: Paul Costello. We have discussed internally three options. One would include a six-month subscription, a one-year subscription, and a two-year subscription, each of which would be renewable upon request.

DR. BRINKER: And the patient can use this as many times as they want?

MR. COSTELLO: Unlimited use, unlimited access to

the 800 number.

DR. BRINKER: And they are charged per prescription, not per use?

MR. COSTELLO: They would be charged per subscription period regardless of use.

DR. BRILL: To answer the other points, we did debate whether or not every strip should be transmitted to a cooperating physician, but it was our determination that -- again, as you know, in a prescreened population, most of the strips you see, you don't need to see, and don't want to see -- and it was our thought that we could provide the service of being the data warehouse for these strips, which we would have to make the decision where not essential that they be viewed immediately, and only again trigger a physician call, just as you are now only being called.

What happens with those other strips, as you know, is they get put in the mail or faxed to you, and if it is over the weekend, you will see them whenever, but they don't require immediate attention. Rather than bother the physician with those things, we will hold them.

DR. BRINKER: I think that that is fine. I just think that you ought to have a physician sign that they are willing to take responsibility if there is a problem, and that is the extent, they are not willing to do anything more

than to be the conduit. But that is something that we can think of later.

I think there should be a better disclaimer, and people have been talking around this, but the fact of the matter is that this service does not replace the traditional physician-patient relationship that is essential for the diagnosis and treatment of cardiovascular disease, and I think that that should be a prominent disclaimer in any advertising and labeling that you have, and if the patient wants to circumvent that relationship, that may be their option, but I think they ought to know that there may be a risk to this, and there is no claim by your company that you would in any way suggest this is an appropriate way for people to react.

DR. BRILL: In Label B, which I personally favor, it actually says twice that this is not a substitute for medical supervision and that it is not a therapeutic device.

DR. BRINKER: Therapy, that is no-brainer, it is not a therapeutic device.

DR. BRILL: To you and I --

DR. BRINKER: It is a no-brainer, that it has to be mentioned, but the issue is that I think that the disclaimer should be so strong, maybe in bold writing somewhere, and that the patient may have disease that is not

detected by this.

Let me ask you a couple of more mundane questions. One is, how many non-analyzable tracings, what percentage of tracings that you receive are non-analyzable?

DR. BRILL: In general, what happens is the patient is asked to re-transmit, so if the question is, that you don't get --

DR. BRINKER: But say the arrhythmia is gone.

DR. FAUST: I would say less than 2 percent.

DR. BRINKER: Some of these arrhythmias must be misdiagnosed initially by the technician. I can't believe that it is 100 percent perfect diagnosis. So what percentage are -- and I know that doctors only overread 1 percent of these -- but what kind of quality control have you instituted to know what percentage are misread or erroneous?

DR. BRILL: I think the answer is we probably don't know now because if you get a strip which you think was erroneously interpreted, you probably don't contact the company with that information. My guess is that you make some corrections on these strips when you receive them for your own records, but don't necessarily call the company back, so I don't think we have accurate information as to percentage of misreads.

As we go forward, when we are screening -- and again on that slide I put this is what we will do -- currently, we don't do the same screening processes because every rhythm strip is reviewed by a physician who prescribes it, so we didn't feel that that quality control was necessary at this point.

DR. BRINKER: First of all, I think that without interaction on the questionnaire, the questionnaire is almost worthless. In other words, somebody says heart attack, writes down heart attack, yes. Somebody doesn't question, well, what do you mean by a heart attack, you know, were you in the hospital da-da-da-da, most lay people don't know what a heart attack is especially if they haven't experience a myocardial infarction.

Be that as it may, is there any patient that you would not enroll based on that? Is there anybody you would say I think you are too sick for this, you should see your doctor?

DR. BRILL: It is difficult to codify all the possibilities that could happen, but using judgment, I would say yes, that --

DR. BRINKER: That is your judgment. I want to know the person who says on a piece of paper, what is your guidelines for saying this patient should not be admitted?

DR. BRILL: If the patient describes that they are having -- we have those sentinel symptoms --

DR. BRINKER: But those sentinel symptoms are questions that you ask when the patient calls. I am talking about the initial enrollment, is there somebody that you would say we are not going to send you one of these because we believe you are --

DR. BRILL: It is difficult for me I guess to conceive -- there is a different issue of whether or not we impede access to physician medical care -- but I cannot conceive of a way in which this device would hurt that patient.

DR. BRINKER: We have gone over some instances where it could be a delay.

DR. BRILL: If it delays, so the question is then not can they not receive the device, but are they receiving appropriate medical care.

DR. BRINKER: Let me just finish.

DR. BRILL: I think they are slightly different.

DR. BRINKER: I don't. I think that there may be -- and I think you guys ought to think about this -- groups of patients that you might consider in the best interests of their care, they not get this except by a physician prescription. So, you can take that home and think about

it.

My final question is --

DR. SWAIN: Jeff, I think we need to go around. We have to break for lunch at 12:00.

DR. BRINKER: Can I just ask my final question? It is like two seconds.

DR. SWAIN: Okay.

DR. BRINKER: You say that physicians are available 24 hours -- well, to supervise -- there is no on-site physician 24 hours a day, 365 days a year.

DR. BRILL: No, there is not.

DR. BRINKER: And there must be a specific algorithm that would ring a need for a physician. So, the question is, what is the algorithm -- you don't have to answer it -- but the thing that I think you are going to have to answer to the agency is what is that algorithm and how quick is the physician response mandated, in other words, can a guy be on the golf course and fall back, within two hours, or does he need to get back within five minutes.

DR. BRILL: I can briefly respond. The real problem is in the in-between, if the patient is having intermitting chest pain, we don't need the physician, the patient goes to an emergency room. The place where we see the physician being most helpful are those who don't fit the

clear-cut criteria that we have already established as needing immediate medical assistance to help decide something where the technician isn't sure how to fit the data into the protocols that we already have.

In terms of availability, we believe that there is a nurse and cardiologist who will be available, and they have to be available within 15 minutes.

DR. SWAIN: Thank you.

Dr. Gregoratos.

DR. GREGORATOS: I find this discussion very interesting. As other panel members said, I think we are dealing with a much more difficult conceptually issue here than simply recommending approval or disapproval of a device.

Now, starting off where Dr. Brinker left, one specific group of patients, for example, that I would want to know whether you would enroll or not is how about somebody who is status post-survival sudden cardiac death and present defibrillator in, and he goes up and he wants to enroll in this service, would you enroll him?

DR. BRILL: The question, would we enroll him without a doctor's consent is the real question.

DR. GREGORATOS: Under the present scheme of things.

DR. BRILL: Under the present scheme of things, yes, we would enroll him, with the labeling saying clearly that this is not a substitute for medical care.

DR. GREGORATOS: I think potentially, you would be doing that patient a disservice, potentially.

DR. BRILL: Do think it is possible we might also be doing him a service?

DR. GREGORATOS: I am not sure, I don't think so, but that is something to consider.

DR. BRILL: Because, as you well know, current defibrillators are ray counters only, although hopefully, very soon they will be more than that, and perhaps we may pick up things that weren't picked up by the defibrillators, which are difficult to read ECGs at this point.

DR. GREGORATOS: But the point is that somebody has a defibrillator is married to his sister, a physician, and the follow-up, and so forth, and my concern is that they may use this as a substitute.

DR. BRILL: We have the same concern, and we certainly would not want them to do that, and other than the declaration on the labeling, I suppose we could have them in the statement say I will not use this as a substitute for my own physician's care.

I share your concern. I don't want that to happen

for a lot of reasons, including the patient's well-being and the liability all around of taking this patient away from their physician. That is not our goal.

DR. GREGORATOS: Something to consider. Okay. I have a whole host of questions that I don't think I will finish the first go-around, and I will take them in no particular order.

The issue of liability. How is your company going to deal with this, and do you think that perhaps if you have a signoff by a physician, this would help you in terms of the liability issues when you have a poor outcome, and so forth?

DR. BRILL: I think yes and no. We currently all have contracts, if you will, with our patients. They come under our care. There are actually federal rules that tell us how we can dismiss them from our care, and although the issue was brought up, well, what if I get a call in the middle of the night, and I didn't expect it, right now we get calls in the middle of the night saying I have chest pain that you didn't expect or I have dizziness that you didn't expect. So, that is not very different from the contracts that we, as physicians, now have with our patients.

If the physician signed off, that physician

already has responsibility for the well-being of that patient, and I don't think, as a physician, or you, as a physician, want to sign off on Heart Alert. That would be a very awkward thing for you to do.

You currently sign off on Heart Alert's ability to monitor a strip, but I am not sure we want every physician in the country to be our partner in that way, it would be difficult. I would have a hard time as a physician saying, oh, yeah, these guys are great.

DR. GREGORATOS: A comment. I am sure you are going to revise your instructional tape, and I would strongly urge that whatever the labeling ends up being, that that be explicated in the videotape, because people can learn much more from this type of an audiovisual presentation than just handing him a written thing.

DR. BRILL: I would agree.

DR. GREGORATOS: Now, the frequency response of the recording device, is it adequate to detect S-T segment shifts or not?

DR. BRILL: No.

DR. GREGORATOS: So your technicians will not be faced with an S-T segment depression or elevation where they will have to make a determination even if you don't have chest pain as an indication?

DR. BRILL: No. We will not be trying to diagnose ischemia.

DR. GREGORATOS: Does the device pick up pacemaker spikes?

MR. COSTELLO: The answer to that is not reliably, so we would not advertise that or list that.

DR. GREGORATOS: Therefore, I would submit that perhaps along with the defibrillator, patients who have an implanted pacemaker may not be appropriate for this type of service.

DR. BRILL: I would agree in many circumstances, it would be very difficult to interpret, I agree for pacemakers.

DR. GREGORATOS: Thank you.

I presume the company anticipates an increase in its business if this thing can take off like wildfire, I mean let's call a spade a spade.

DR. BRILL: It has crossed my mind.

DR. GREGORATOS: You have the resources and the number of technicians and telephone lines, and so forth, or there will be queuing of telephone calls?

DR. BRILL: A new telephone system was installed, and obviously, assuming approval, we would make those advances. No, we haven't hired all the technicians ahead of

time without knowing that we have approval.

DR. GREGORATOS: But you are prepare to handle that sort of thing?

DR. BRILL: Yes.

DR. GREGORATOS: I am also very concerned about what has been brought up by every other member of the panel about whether this device can be actually used to delay urgent medical care, and somehow in the labeling, in the instructions, and so forth, it has to very explicitly stated, I think, above and beyond, that this is not a substitute for going to your physician.

There will have to be specific indications to where if this happens, you should go to an emergency room, don't rely on the device, that sort of thing.

DR. BRILL: We share that concern entirely. That is why we came up with that list of symptoms. It is likely that, if approved, someone will be delayed somewhere. If we see 30,000 patients, it will happen to someone.

On the other hand, it is also likely that we may pick up some valuable information that may also be extremely beneficial, but I am sure that whatever we do, we can't eliminate that potential, and all we can do is try our best to make sure it doesn't happen.

DR. GREGORATOS: Going to Item B6, the enrollment

form, the issue of the medical history that you acquire at the time of enrollment, does this factor into the protocol, to the algorithm, in other words, if a patient who has had a previous infarct, as I follow it, the technician has a different algorithm than somebody who is having an arrhythmia without an infarct?

DR. BRILL: No, we considered trying to make algorithms for every medical condition and when we started working on it, it became just untenable. The symptom list we have is extremely conservative. Any persistent system gets you a trip to a doctor or emergency room, or contact a medical facility.

What we have tried to do is make our criteria so strict that we will err on the side perhaps of sending someone for medical attention they don't need, but that we will not err on the side of denying them medical attention when they need it.

DR. GREGORATOS: A technical thing. Many patients, elderly patients, and so forth, do they have any difficulty changing batteries, and so forth?

DR. BRILL: It is a thin battery. It is relatively simple, but yes, it is one of the hearing aid type batteries, and it could be difficult for some patients. When they get the kit --

MR. COSTELLO: The company anticipates not only sending in the original subscriber's kit, extra batteries, which the subscriber can then change themselves. We have also reviewed the ability of the company to replace batteries for individuals, for example, this device gives an indication of battery depletion far in advance of the battery actually depleting.

Our technicians will be able to readily detect this at each ECG that becomes transmitted when the battery falls below a certain threshold. If someone is manually incapable of changing a battery, we have discussed amongst ourselves the possibility of perhaps swapping out that device with the individual, providing them with fresh batteries.

DR. GREGORATOS: That was my suggestion, that some elderly patients, it may be easier to just ship them a new device and have them ship you the old one back.

MR. COSTELLO: In some cases it would be easier than actually changing the battery.

DR. GREGORATOS: Thank you. I think that is all I have for now.

DR. SWAIN: We can start with Dr. Tony Simmons' questions for the next five minutes, and then we will continue after lunch.

DR. T. SIMMONS: I guess I have a significant problem frankly. I feel like I am not exactly sure what the heck it is I am asked to approve here. I have got so many revisions and changes, and some that aren't even here, that have been on the blackboard.

I find a lot of anxiety here. I have no idea exactly what it is you are proposing. I also have a tremendous amount of anxiety about how prepared you are for today. I would have thought that very important questions have been brought up about what is it you are going to tell the patient when they call in, and what I am hearing is, well, we haven't decided, but we will think about it.

I think that is a very important issue. Let's go back to the patient that we talked about, the patient with the PVCs that you see every day. I see those patients every day, too. The fact is, unfortunately, we run our own monitoring service, so I have to read these strips every day, and at night I go home and take these things, and I end up with a garbage can this tall of the strips that I have just thrown away where I have culled out PVCs.

I want to know what you are going to tell that patient. The fact is I am not sure I even like these words you are using, "patient." It is your customer, it is my patient.

DR. BRILL: Right, a subscriber, absolutely.

DR. T. SIMMONS: So, I would like to know what it is you are going to tell my patient when he is calling with those PVCs and what you are telling me is I don't know, and I think that is a serious problem right now.

DR. BRILL: Our initial intent --

DR. T. SIMMONS: Let me finish.

DR. BRILL: Oh, I am sorry.

DR. T. SIMMONS: Because, number one, you are saying you think this is going to alleviate this patient's anxiety, and I am saying I think you are going to make him much more anxious because every time he calls in, you are going to say, yes, you did good, you have PVCs, you have got to run back and go tell somebody about this, and I think you are going to be playing into patients' anxieties, and I think that is a serious negative benefit. I mean I think that is a risk that you have not addressed.

So, if I have to answer the question right here, is this safe, I am going to say, no, it's not safe, the fact is you are going to make many more patients anxious than you are going to relieve, and you are going to send many more patients to the physician who don't need to go to the physician, and you are going to delay patients getting medical care when they should get medical care.

I don't think you have identified your patient population at all that might benefit from this. I am having a real major problem here.

DR. BRILL: First, I would like to apologize for some of the last-minute submissions. We were receiving some faxes even over the weekend, and so some of the things, not preparedness, but some of the items we have for the board were only prepared over the weekend as we got some responses to labeling.

The first question is who is going to go out and get this device. We are not going to send this like America Online to your house and say, hey sign up for this.

DR. T. SIMMONS: You guarantee that.

DR. BRILL: I guarantee that.

DR. T. SIMMONS: I don't believe you.

DR. BRILL: It's a $700 --

DR. T. SIMMONS: Can I ask the FDA is that something that you can guarantee is not going to happen, that these aren't going to appear in grocery stores somewhere? I mean is what they say here on this microphone legally binding?

DR. BRILL: I guarantee we will not mail these to people's houses unsolicited.

DR. GILLIAM: How about the application for them

unsolicited?

DR. BRILL: Well, the FDA is supposed to assist us with whatever advertising we develop in the future. That hasn't been developed by us or by the FDA, so I am not prepared to say exactly what the FDA wants and what we want.

DR. T. SIMMONS: Well, let's go back to the patient who has PVCs, who is very anxious, and I have just spent an hour in my office calming him down and saying you are going to have these, be very careful, just get up, if you have more symptoms, give me a call, and now you are telling him, yes, you have got PVCs.

DR. BRILL: And you have told him several times this is okay, it is PVCs, so then he calls us up, he or she, transmits PVCs. What do I have? You have PVCs. Dr. Simmons told me I had PVCs. He said I don't need to worry about that. Is that creating more anxiety or reassurance?

DR. T. SIMMONS: I think it is creating more anxiety because now he is focusing on them. I have told him not to think about it, not to react to it, to ignore it, and you are telling him, yes, they are there, keep on calling, and so you are telling him, you are teaching him how to feel his PVCs, you are teaching him how to focus in on his heart, so now every time he calls in and you say, yes, that is a PVC, no, it wasn't one there. So now he is learning very

carefully when he is having PVCs.

Now he is really focusing in on his PVCs.

DR. BRILL: What if he was really focusing in on his PVCs before we came along, and he was just calling you, and you just kept telling him it's okay, it's okay.

DR. T. SIMMONS: So you are saying now you are going to take care of bad doctors.

DR. BRILL: No, you are not a bad doctor.

DR. T. SIMMONS: What are you saying?

DR. BRILL: I am saying that that patient may be reassured because I know Dr. Simmons is a smart doctor, but I am not sure these really are just PVCs, I know he saw them before and they were PVCs, but how does he know that what happened to me tomorrow are PVCs.

We can tell the patient, yes, it was just the same PVCs that Dr. Simmons diagnosed, that is what you have right now. Is it going to make them -- yes, some people may concentrate more on this than they wouldn't, is there harm coming to them for that? I am not sure that there is. Is there relief coming to patients who otherwise just get tired of calling Dr. Simmons who says don't worry about it.

You may think because they are not calling you anymore that they are satisfied. They may just be sitting home saying, well, I can't bother Dr. Simmons again, but I

still don't know what these things are.

DR. SWAIN: Do you have any more followup to that point before we break for lunch?

DR. T. SIMMONS: We could break for lunch.

DR. SWAIN: We are going to reconvene at 1 o'clock. I remind the panel members that we have a closed meeting about some other topic here in one of the side rooms over lunch, and see you at 1 o'clock.

[Whereupon, at 12:01 p.m., the proceedings were recessed, to be resumed at 1:00 p.m.]

AFTERNOON PROCEEDINGS

[1:00 p.m.]

DR. SWAIN: The male Dr. Simmons is on the telephone right now I understand, so I will ask female Dr. Simmons to start the questions.

DR. J. SIMMONS: I must admit that I agree with all of the panel members who spoke earlier, and I guess as probably the only primary care provider here on the panel, as I am listening, and I am also making an observation, I would probably be the person to see the patient first or hear that patient first, particularly with this complaint, and I am wondering what -- I don't really see what this device will provide that is different from everything else that is out there.

I mean I don't really see the purpose, and I guess my concerns really deal with a quality of care issue, and I have three observations that I am now thinking about and I think most of them have been addressed before.

One deals with the observation that your customer, my patient, must sign an agreement that there will be a provider or facility involved. I have a little bit of concern about the facility. I know in Miami, that facility, if a patient is Miami filled out that form, that facility may be Jackson Moore Hospital.

Well, I mean with the employee population of thousands, who will this patient be directing this information to, I mean who will you be sending this monitor to, because there is not going to be anybody there that is going to bear the responsibility for that, particularly in a large tertiary emergency room system.

So, I am a little bit concerned about that in that it is just very vague, and you could be a physician or facility. Also, I am also a little bit concerned about the fact the sentinel symptoms, and I wasn't really sure, when the technician gets the symptoms, they are going to tell the patient to call that referring person or institution, and I am a little bit afraid.

Here again, I think it was mentioned earlier that there will be delay, because I mean we have patients that come in all the time that should have gone to the emergency room, I mean should not have even called me, but should have gone to the emergency room, and I think those three or four symptoms may fit into that category, so you are going to delay needed care, emergency care.

The other concern I have -- and these are all quality of care issues -- the other concern I have, and it was mentioned earlier, about the indication depression and also athletic disease, and I can see everybody who is in the

Gold's gym, wanting to buy one of these. I can just them walking around the gym with one of things on their chest.

I am a little bit concerned about those indications and whether they really should be there.

I can't really say if it will work. We really don't have that type of information, but I am concerned about how it is interfacing with the patient and with the provider, and the followup, there needs to be some continuity of care if there is a problem, and I don't really see that here.

DR. BRILL: I will try and address all of those issues. You stated that this doesn't seem to really be different from anything that is already out there. That is our contention also. We want to make it very clear that Heart Alert has been operating a high-quality monitoring service for 10 years, and this is no different from that.

What is different is the way in which people will get into the system. That is the major difference. You talked about what is going to happen if somebody sense a rhythm strip to -- I will give my local reference -- Johns Hopkins emergency room. That is why we decided that we would not send every rhythm strip, those of no consequence, to the emergency room, because they will have no idea what to do with it.

Our point is to be a triage. When that person calls, if they meet our criteria for immediate medical attention, that is when that strip goes to the emergency room, that is when that strip goes to a physician if that is what the patient has designated, and that is when the patient or we initiate the call for medical assistance.

So, the data won't be piling up somewhere, it will be kept at Heart Alert for future reference should somebody want that information in the future, but the strips, which we determine do not require immediate intervention, will not be sent out.

You mentioned quality of care issues. Again, these are the same technicians and the same monitors and the same devices which are currently in use. You may well get a patient who comes to you complaining of palpitations, who for some inexplicable reason to you has a strip of what they were. I don't see how that harms the patient. I think it might make it easier for you to treat that patient.

You might on your very first visit say, oh, yeah, that was a PAC, no big deal, and you don't have to have them wait another 30 days. I am only saying that I don't see the harm in that. I think there may be some benefit to that, but I certainly don't think that the individual is somehow hurt by having this information, which many of us as

physicians would say I don't really need to know that.

What we are doing is we are giving the individual the ability to get some information on their own. We will tell them that we will let you know if this is a serious emergency situation, and we will help you get help.

If it is not a serious emergency situation, much like in other things where one has blood pressure, glucose monitoring, HIV testing, people are given some information, but it is up to them to follow up on the information as to what they want to do with it.

I don't know if I answered all of your points.

DR. J. SIMMONS: I think so. I am still a little bit concerned about that last issue. They do have the responsibility, they are empowered to do something about it themselves. I mean you are giving them the information, but I am a little bit concerned, particularly in this day and age of primary care and quality assurance, are we going to get the followup that we need.

We have someone out there that needs to go to the emergency room, are they going to go, or we have someone out there who -- because all this is telling you is that they are going to put my name down and say I am their provider, but we have no way of knowing that they are going to actually get the care that they need.

DR. BRILL: The alternative, as they would stand now is they may or may not decide. It seems more likely to me that if we say to them this is a serious thing, you need to get medical attention, that they will do it than if they are sitting at home saying I am not really sure this is anything, maybe I won't bother. I think it unlikely. They may be just as likely on their own to seek medical attention, but I don't see a scenario in which they would be less likely to seek medical attention because they use our service.

The other thing is, again, we get back to the immediate response. If one of your patients calls you, there is a delay, hopefully, a short delay, but there is a delay. That 800 number gets answered within two minutes. There is an immediate response.

Would it have been better for them to call 911? There may be a one-minute delay there. Could that be crucial? I don't know if a minute counts.

DR. J. SIMMONS: Some of us have identified patients that we tell to go to the emergency room, but what I am a little bit afraid of is you are going to have a level of comfort out there with a device you can just buy over the counter, that says, okay, I can go through these different steps before there is that 911 call, and that is a little

bit disturbing because we see it all the time, particularly the family practitioners and the internists who actually are practicing primary care. I mean there is patients that come in all the time who should not have come to me first. They should have gone to the emergency room first.

When I was listening to your description of the different sentinel symptoms, and I think you said that the technician will tell this person to call that referring institution or provider, well, that is minutes that is lost.

DR. BRILL: The question is -- and I don't think any of us can measure this -- if that patient or person were otherwise inclined to immediately call 911, they would get a faster response by a matter of a couple of minutes probably, I agree -- the question is are we also going to find some people who would not call 911, who we pick up otherwise and help refer them to a medical facility. I don't know the answer to that.

I think there are patients on both sides of that. I am not sure that a two-minute delay is a serious delay when my guess is there are bigger delays than that in the system, but in terms of the bottom-line question, are we going to be keeping people from getting medical attention, that is the primary goal and concern and ours, is not to let that happen, and any input we can get -- we believe it is

possible to do this and not have that bad consequence.

DR. SWAIN: You probably would be careful what you are advising. You know, the big point here is that this is diagnosis, not treatment, but you have just implied that the 800 number may get a quicker answer than the physician, so the initiation of treatment, which is go to 911, you are implying that you are going to, in fact, make this a treating system, not just a diagnosis system.

DR. BRILL: A triage system.

DR. SWAIN: No, treating. So, I assume you are not implying that this is a treatment.

DR. BRILL: Well, we are not going to dispense any therapy.

DR. SWAIN: Right, but telling somebody to go to an ER or call 911 is initiation of treatment, so are you saying, in fact, that this device -- "device" meaning the system -- is not only diagnostic, but is treating?

DR. BRILL: Am I saying we will refer them to emergency rooms on occasions? Absolutely.

DR. SWAIN: So you are talking about treatment.

Did you have any other questions?

DR. J. SIMMONS: No, the only observation was the depression, and I just thought that was a little bit inappropriate as an indication.

DR. SWAIN: I think the panel members, especially new panel members, if you have a specific question to ask, you can answer a specific question, but you can't comment on a comment. So, please answer any specific questions addressed to you.

Do you have any specific questions?

DR. J. SIMMONS: No.

DR. SWAIN: Do you have any other comments or questions?

DR. J. SIMMONS: No.

DR. SWAIN: Dr. Tony Simmons.

DR. T. SIMMONS: Sorry, I was trying to change a plane reservation.

First of all, it was pointed out to me that when I was asking some questions before, that I had said that I did interpret these strips, and there was implication maybe that I have some interest in a company that sells or markets these things, and I do not. I get no financial reimbursement for -- like all electrophysiologists, I see tons of PVCs and rhythm strips, and the hospital does Holters and things like that, but I do not have a part interest or any financial interest in any monitoring system. I wanted to make that point.

Let me just go back to the point that I was

actually talking about before. I guess maybe it is the key point, you know, what is the population of patients that you are going to be selling these things to.

I want to hear you say something different than what I have heard you say, and that is, a person comes and fills out one of your forms and says on your form I have coronary disease, I have had a myocardial infarction, and I have had fluttering of my heartbeat, and I do feel near syncope, are you going to sell him this unit, or are you going to say, for God sake, go see a doctor?

DR. BRILL: Both, which is what we do say in the labeling. Yes, we will sell him the unit, and yes, we will say this is not a substitute for medical care.

DR. T. SIMMONS: See, I don't think you should do that. I think you should say you need medical care, you do not need an impersonal person somewhere off monitoring because even on your own labeling you say that whether or not you find an arrhythmia, that person needs to be seen by a physician, and by providing him with this monitor, you are implicitly saying that this is okay, we will help take care of you. We think you are wrong, but we are going to help take care of you. And that is wrong.

You should put the emphasis back on the patient. You know, the first rule is do no harm, and so you should

not sell the device to somebody that you are going to potentially harm. So, if you have a patient with congenital heart disease, if you have a patient with coronary artery disease, if you have a patient with syncope, if you have a patient with palpitations, and things like that, they should be refused and sent off to their physician for care, not commercialism. That is my point.

DR. BRILL: Is that a question or a comment that I can't respond to?

DR. T. SIMMONS: You are welcome to comment on that.

DR. BRILL: That same patient who has all of those medical problems and has been evaluated by you and properly treated by you --

DR. T. SIMMONS: How do you know that? What are you saying? This guy filled out a form. The guy filled out a form, and he has come to buy this --

DR. BRILL: How does he know he has coronary artery disease and he has a defibrillator?

DR. T. SIMMONS: Five years ago he had an infarct, and now he has got palpitations, and he is almost passing out, and he sees your advertisement in USA Today and decides he wants one of these things.

DR. BRILL: And he is just not to come back to

you?

DR. T. SIMMONS: No, he has not needed to come back to me until now.

DR. BRILL: He is passing out and having palpitations.

DR. T. SIMMONS: That is right. You should send him to somebody.

DR. BRILL: Well, he has already decided not to see you.

DR. T. SIMMONS: No, he may not know enough to go to somebody.

DR. BRILL: By definition of your question, he has not come to see you, and the question is, is there now some danger because he has decided, although he doesn't want to see you, he does want --

DR. T. SIMMONS: No, you are providing him with an alternative to going to the physician. He has not decided, you are helping him decide. If you are not there, he would hopefully go to his physician.

DR. BRILL: So if Heart Alert were not providing this service, what would happen to that patient?

DR. T. SIMMONS: Hopefully, he would go to his doctor. Hopefully, if he comes to you, you will reject him and tell him go to his doctor.

DR. BRILL: Will we accept him and send him to his doctor?

DR. T. SIMMONS: Or will you accept him and he will die in his sleep that night because you provided him with a little card that said, oh, this is my little protector here, I will put this on my chest tonight.

DR. BRILL: Now, we accepted him and referred him to his physician, and I presume you saw him that day.

DR. T. SIMMONS: Did you refer him to his physician or did you just let him buy the card?

DR. BRILL: Well, you just created a difference, and I said we would accept that patient and refer him to his physician. My question is what harm comes from the diagnostic device as long as the patient gets appropriate medical care.

DR. T. SIMMONS: Because the diagnostic device provides him with a level of assurance that is inappropriate.

DR. BRILL: And in your opinion, there is nothing we can do. There is no point in my answering that question in terms of insisting and advising the patient to seek medical advice.

DR. T. SIMMONS: I am sorry, I missed that point.

DR. BRILL: I get the feeling that whatever I say

in terms of what we may do to spell out to the patient that it is no therapy and that they need to see a doctor, that you don't think that will be adequate, is that correct?

DR. T. SIMMONS: I think that's right. I think you need to send that patient to a physician, and not try to provide the care through a technician in another state. It is your obligation do no harm, do the right thing, send the patient to the doctor.

DR. BRILL: In our mind, it is not either/or. In your mind it is. That is our difference.

DR. SWAIN: I think that is a good summary. I think that is 10 minutes and we will keep going around. Dr. Weintraub.

DR. WEINTRAUB: This is very educational. I think I got most out of reading the ACC-AHA task force on ambulatory electrocardiography, and I was rather amazed, not being particularly educated in EP, at how many things fell into Class III, that is, in which ambulatory monitoring is not really thought to be helpful.

I am not going to read them all, enter them into the record, but if you look on page 211, basically, stable coronary disease, asymptomatic microvalve disease, asymptomatic patient with known heart disease on an exercise program, assessment of risk for potentially disabling

arrhythmias, and on the next page, patient with known stable coronary disease without evidence for myocardial dysfunction, asymptomatic patient with known heart disease, et cetera, et cetera, and then on page 213, patients with atypical chest pain, chest pain atypical for myocardial ischemia, et cetera, really rules out a hell of a lot of patients, a great part of the population.

I am now going to ask you questions which I think staff are going to have to direct me as to whether they are appropriate or not, and I am not asking them because I want reply to every information, but I am asking them in an effort to try to define the population of patients that you are going to market this for.

So, I guess what I am going to ask you for first, I don't think you would have gone through this, and the expense of doing all of this and modifying the card, and all that, unless you had done some market research.

So, you must have some market research, and you must have some idea of your target population. Can you describe that for us?

DR. BRILL: I will defer to Mr. Costello.

MR. COSTELLO: To give you an idea of the market size, we anticipate the market to be in excess of 10 million individuals.

DR. WEINTRAUB: Again, your market research must have shown you who were the potential customers.

MR. COSTELLO: Right. Without giving too much away here, predominantly symptomatic people again with those symptoms suggestive of arrhythmia.

DR. WEINTRAUB: Patients with palpitations.

MR. COSTELLO: As we showed a slide earlier, in the 1991 study, there were 13 -- I believe it was 13, perhaps 12 million physician visits for symptoms suggestive of arrhythmia.

DR. WEINTRAUB: Does that include patients with chest pain?

MR. COSTELLO: No, there was no chest pain per se. They were all predominantly palpitations, lightheadedness, tachyarrhythmia type of symptoms, and of those 12 million visits, arrhythmias were found to be the cause, I believe, 708,000 times.

So, looking at that statistically, 7 percent or so, ballpark mathematics, 7 percent of those symptoms were documented with arrhythmias.

DR. WEINTRAUB: Let me come back at you with another question. Again, I am not asking this question because you want you to divulge proprietary information, again, I am trying to pin down some idea of the population,

the target population.

So, my question is give me a ballpark in terms of what this subscription would cost the average person.

MR. COSTELLO: We anticipate it to cost no more than -- we anticipate the device to cost no more than what the device would currently cost a physician today. It is a nice way of saying --

DR. WEINTRAUB: That's fine. What is that today?

MR. COSTELLO: The retail price of this device to a physician today is in the neighborhood of $850. We would anticipate it be significantly below that.

DR. WEINTRAUB: And that would be for a one-year subscription?

MR. COSTELLO: That would be to own the device. It would be our intentions to be able to be selling these devices and communicating to the individual that the device is useless without service, and selling service subscriptions in addition to that.

We would anticipate the subscription to cost no more than the average cost of one test in a physician market today, which is anywhere from $250 to about $600 depending upon third-party reimbursement.

DR. WEINTRAUB: Now, finally, do you foresee the subscription as being reimbursable by insurance, any part of

this reimbursable by insurance?

MR. COSTELLO: We have not discussed that internally, but we have gone on the assumption that it is not.

DR. WEINTRAUB: With all of this discussion, and again I am just sort of trying to very briefly summarize in my own head, that if a strict constructionist, and I look at it in the purview of the FDA, and I think if I am being absolutely strict in my own mind, it is sort of hard for me to reject this proposal on the basis of safety. Again, this is strict construction, the device itself is not harmful.

There have been safety issues raised, and I think they are legitimate, but in terms of the device itself, and the transmission and all, that is pretty safe. Efficacy, from the data presented, I have to conclude that the device and the system does what it says it is going to do, that is, it picks up arrhythmias. What one does with that information is a completely different question, but it does seem to be efficacious in the sense that it picks up those arrhythmias in a high percentage of cases if the 2 percent loss rate is correct, which I am a little suspicious about, but let's say it does in a high percentage of cases, then, it would be at least again strictly constructed to be safe and efficacious.

If we say that the device ought to be approved on that basis, then, I think the safety issues and all the other issues really, as Jeff Brinker said, really have to be pinned down on the basis of labeling, and that is why I think Dr. Spyker was so emphatic about it. I think the labeling is critically important, and although I agree with Alternative B being the best alternative, I think that if it were to be approved, that ought to be the basis of labeling, but I think it could be even tighter, and I think that it really ought to be absolutely laid down that a physician be involved, and the complexity of dealing with arrhythmias should be explicated a little bit more.

Again, if you are aiming at a seventh grade level, this is difficult, but I think that the customer should understand that this is a very complex business, and that what may be benign in one patient, may be very dangerous in another, and vice versa, and that really only physicians trained in this area can give a complete assessment.

I think that got be part of the -- if it is approved, I think it has got be part of even a tighter labeling.

That is really all I have to say.

DR. SWAIN: Dr. Vetrovec.

DR. VETROVEC: I want to go back to the physician

issue that the patient lists, and I would argue that the physician should be notified that that patient listed him for the following reason. Suppose a lady lists her obstetrician as her primary care physician, that individual one could easily argue may not be qualified to interpret that data if it were sent to that individual.

They should have an opportunity to say, hey, I am the wrong guy before there is a 911 emergency. So, I think the doc should be, not so much the signoff from a medical-legal aspect, but from the standpoint of am I qualified.

The other thing that could happen is the patient could put down the name of a doctor that they haven't contacted yet, that is not taking new patients. So, when the call comes in the middle of the night, he says this isn't my patient.

I think some closure of that loop needs to be made, not from a medical-legal standpoint.

I would also wonder, since you are talking about two-year contracts, what updating is going to be made on the medical information. For instance, regarding drugs that might be important or new symptoms or new events that that happened to a patient. I would wonder what you would comment about that.

MR. COSTELLO: Well, as part of our internal quality control process, if we do not hear from a subscriber within a 60-day period, we will contact that subscriber to essentially establish three basic points:

Number one, that the subscriber still realizes that they can have access to this 800 number; two, that their device still works; and three, that there has been no dramatic change in their medical condition or in their records.

That is not so terribly different than what we currently do in a physician-prescribed service. If we do not hear from a physician-enrolled patient within five days, we generally assume that the person gave up on the test, and no longer uses the device, so we call them up, and we say are you still using the device, do you still know how to use it, are you still committed to using, and to try to reinforce that with the patients.

So, our software and our database has the capability to cue us to individuals who we haven't spoke to at various intervals, and it is already something that we currently do, and we anticipate that would be a natural extension to our subscriber service.

DR. VETROVEC: Any comment to what I just said a minute ago about the doctor that might not want to be the

patient's doctor or not be appropriate?

DR. BRILL: I think you raise a good point. I think it would inappropriate to have an obstetrician or a dermatologist involved, and inappropriate to have, although we do say on the form -- I believe we say that -- I have conferred with the designated physician or medical facility. So the option of not having them -- that is in there on page 20. So they certainly would be informed, but you are right, it might not be the appropriate physician, and I think we have to take some steps to make sure that it is an appropriate physician.

DR. VETROVEC: One more question I have is, is that your technician mentioned earlier that there was a 2 percent inadequate information, but on the current system, but was that based on using wrist electrodes, do we know what the reliability is in terms of transmission of data using the foot system that this will have?

DR. BRILL: That data is based on all of the different modalities that Heart Alert uses, which includes wristwatches and lead systems. Instromedix, I am sure presented that data when their device, which this is predicated on, was approved. I don't have that number in my head.

DR. VETROVEC: That is all I have.

DR. SWAIN: Dr. Gooray.

DR. GOORAY: I sort of find myself in an unusual position. I am the consumer rep, so I am probably one of the potential users of this, and of course, I can't close the umbrella of being a physician.

There are two concerns I have. One of the things I think you spent a lot of time on is supposedly this device is going to increase the access to care. Am I wrong in making that assumption?

DR. BRILL: That is right.

DR. GOORAY: If we predicate this assumption that this thing increases the access to care, when you look at the numbers you present, the people that are potentially going to use the device probably already fall under physician care. Would you say that is wrong?

DR. BRILL: I would say there are people in and out of that population. I would say many of them would, but many of them who have simply the symptoms, such as palpitations or racing heart may not be under a physician's care.

DR. GOORAY: But most of the people you are going to target, if I am a consumer, potential consumer, and a device like this, this kind of thing, I don't know where you are going to advertise it, or how you are going to get your

patient population, but I will make a simple assumption that the means by which you use to advertise this stuff is going to be areas that are accessible to certain people with a certain level of education, which means that implicit in that, is the fact that the majority of these people are already under some physician care.

I make the point that you are not necessarily increasing access to care because implicit in that statement is the fact that when you say something increases access to care, you are broadening your population base, and you are not doing that.

DR. BRILL: I think I understand your assumptions, and I don't think we will know until -- I agree that some of your assumptions may be right. This has not been done in this country, and I suspect there are patients who are not seeing a physician who will enroll, but we haven't done the kind of research that can tell us, of those interested, how many have physicians and how many don't.

DR. GOORAY: But if you even look at studies that have been done say in ambulatory care monitoring, and the analogy was made a lot about comparing this to blood glucose device or a blood pressure device. We know for a fact that there are very good long-term studies to show that ambulatory care and blood pressure measurements are a better

reflection of the long-term outcome of people. We know that, that is well defined. In a device like this, we don't know anything about what its potential benefit is.

We are saying it has probably some benefit is a sense of people become more aware and they are going to seek medical help based on whatever you are doing. Pardon the pun, but I think what we are doing is if you are going to crystallize all this stuff and tell a patient, look, you have asked them all these questions, and I am coming in and I have got all these problems, I have seen a doctor, I have got palpitations, and getting back to Dr. Simmons' idea, is that I have got all these problems, and I am telling you I have got all these problems, and I am crystallizing all this, and as far as I am concerned, that shows me that oversimplifies the overall problem that a patient has, and it gives them -- and I would emphasize the point again -- if I am a patient and I deal with this thing every day, it gives me a false sense of security, and that to me is dangerous.

If we are going to say that risk is worth it, with the potential benefit of increased access to care, I think we are only giving the care to people that already have care because of the very nature of the device, and maybe you can elucidate the point of how you are going to get this, in

what form you are going to advertise this -- I don't think that is a fair question -- because that determines your patient population that you are going to go after.

DR. BRILL: Well, we couldn't prepare those materials because so much of it hinges on the recommendations of the FDA that to try and create that ahead of time would have just been guessing. It depends on what we all agree on are indications and contraindications, so we don't have that material.

DR. GOORAY: I don't have any other questions.

DR. SWAIN: Dr. Goggins.

DR. GOGGINS: I think I don't have anything more than others have said already. I guess I hear the question, the device works, that is not what is being asked today, but what we seem to be asking is how much can individual humans not trained in medicine do independently to care for themselves.

There are kits available. We have talked about them a bunch of times - glucose, pregnancy test kits. You can buy stethoscopes in children's catalogs now to listen to your heartbeat. If these people don't subscribe to this device, what is their fate?

I think you have said this, you have struggled to say that several times already. Would more people be better

off if this device is available than if it is not?

DR. SWAIN: A large philosophical question. Do you have a comment on that?

DR. BRILL: We think more people would benefit, and it is obviously difficult to prove, but again, we look back at this device, we are taking the same service which most of the people in this room use, we are broadening it to allow people to obtain the device themselves. So, the question is does that spread of information create a problem.

We agree with those who have said you cannot let this inhibit a patient's access to regular medical care, and it is our contention that we can do both things, that we can make sure they are referred to the proper physician, and at the same time, provide them with monitor.

DR. SWAIN: Thank you. I guess I have the next questions.

I think this is sort of a unique device meaning a system, as Dr. Spyker says, that we are asking to judge a device based on, as far as I can determine, no data whatsoever, knowing of course this device is only peripherally related to arrhythmia services that are in existence.

There were six patients mentioned in this, only

one of whom we heard about, which was a lady that there is a couple of EKG tracings on, and half of the patients used the device incorrectly, upside-down. So I guess I have a big philosophical question for the FDA here about why we are looking at something where we have no data.

The comment to the company about this is in seven years, I think this is the first time in a panel that I have been on where the company has not had testimony from recognized experts, in this case it would be electrophysiologists, that don't own part of the company or the company, which I think is perhaps not a good trend or perhaps not in the company's best interest for future reference. That doesn't work as well than with recognized experts.

As far as I can tell, I don't believe there is anybody I can tell in this country that would be excluded by the indications here. I think everybody in the world has been anxious or depressed at one time, has a history of heart disease. People's hearts, all the relatives who died had their hearts stop, so it is cardiovascular disease.

Let me ask you one thing. There is no age mentioned. Can a five-year-old go across the counter and buy one of these little suckers and subscribe?

DR. BRILL: No.

DR. SWAIN: Also, there is no mention about other visual or hearing handicaps. If you can't hear the buzz, you can't start it. If you can't see it, you can't start it.

DR. BRILL: In the labeling, it does say if you cannot use the device and dial a telephone.

DR. SWAIN: Well, the manual dexterity, I implied that, so I think that there are other classifications of dementia, of hearing, and all that.

I am very concerned about the lack of protocols. It is sort of build it and they will come, and we don't have any of the protocols that I believe would allow me to judge on this device of who is going to be referred when, and I have the same concern Dr. Simmons has about delay of care to the wrong physician, the OB physician, and I have exactly the same concerns about who will accept these patients.

You know, somebody could put down my name I have never heard of. It is unlike the current device where it is a physician contract with your company, and that is a big difference, and likewise having spent some time at Jackson Memorial or any other university hospital, I have no idea who would get notified or perhaps in any system who might care about or know what to do about this.

Those were some of my concerns.

You mentioned you had no QA. I guess it wasn't needed before.

DR. BRILL: No physician overread QA because every strip was read by a physician.

DR. SWAIN: Right, which is kind of a funny way out of that one in that you have already said that the physicians very often don't read them or don't call back, so you have said that QA is the physician, but you recognize the physician doesn't tell you when you read them wrong. So, I assume there is a plan.

DR. BRILL: We outlined it.

DR. SWAIN: That is one of the other problems I have. I will talk to the FDA about the data we have, but I would hope the FDA would be concerned about a bomb-proof QA plan.

DR. BRILL: We talked about the 10 percent overread by supervisor, and 1 percent overread by cardiologists.

DR. SWAIN: I guess if I were an EP person subscribing to your service, I would be asking that question about the present service.

How do you plan to deal with the same problem all the software designers have? I buy one unit, and pass it around to my buddies. If they think they are having a few

problems, they can slap that on there.

How do you have the integrity of knowing that the only user will be the person who bought it, who filled out the questionnaire?

DR. BRILL: Well, when a person calls in, they are asked to identify themselves. Certainly, they could lie. We can't keep people from taking other people's prescription medicines, driving other people's cars, drinking other people's liquor. There is no way. If people want to lie and use subterfuge, they will, and I don't know of any device or system that can prevent that.

DR. SPYKER: They would sign a card.

DR. BRILL: That would help, although I would hate to base my judgment on that. Theft and fraud are rampant, and I don't know that we can solve it any more than anybody else can.

DR. SWAIN: That is the end of my questions. We have an adjourn time of 3:00 p.m. today, and I am going to ask the panel to go around again for any further questions, but in particular, there are I think five questions that the FDA has come up with, that they wish us to address, and I think that we need to go around and see who would want to address any particular point on these.

As I implied, I have an extremely hard time

finding who this device should be used by. I think the A, B, and C, you can take all these people with known cardiac disease and all that, and I think there would be people that aren't eligible for use of this device, and the same question I think Tony brought up or Jeff brought up about increasing anxiety, the worried well.

I think at the initial pass, I would think this would be something for the worried well except I think we would make the worried well even more worried. So, I am kind of in the population where I can't imagine what population I think this device is for, but I wish each of the panel members to ask any further questions and to address anything they can of these comments.

Anne is first.

DR. CURTIS: I was going to make a similar comment about the worried well, so it has already been made. I think the people we don't want to use it are people who have known heart disease. Maybe the patient is more prone to have arrhythmias, but I think that is where the danger comes in more.

In terms of the labeling, I think we easily agree that A doesn't work. In terms of B and C, I actually like the indications in C better because of the bullet form, but what I would do is I would at least throw out the last

three. I would throw out the coronary disease, chest pain, and heart failure.

I think the business about history of arrhythmia that was brought up before is true. It is kind of odd to have it as an indication and a contraindication, and I am not quite sure what the best way is to handle that.

The problem with the indications in B, I think are that they are true statements, but kind of vague in terms of somebody deciding whether or not to use the device. The fact that you can have serious rhythm problems without any sensation, well, that is true, and that probably push somebody to get an event monitor just to record willy-nilly when they are not having any symptoms at all.

In the second paragraph there that talks about you might benefit if you have heart problems related to an irregular heart rhythm, well, what kind of symptoms are they, and the average person with a sixth or seventh grade level of understanding, I don't think knows what kinds of symptoms could be related to heart arrhythmia and which don't.

So, I think they are all very true statements, but not very helpful in terms of a labeling indication. So, I think that the C actually works better for that, if you have got a racing heartbeat or palpitations or whatever.

In terms of the contraindications, though, in a way I think you need some combination of the B and C contraindications because, obviously, you have to be able to get the device on your chest, and if you can't do that, you can't use it, and the fact that I think there is more of an emphasis in B on the device not being a substitute for medical attention, I think that works a little bit better.

On the other hand, in C, I believe that the fact that it mentions that you should consult your physician if you already have a history of cardiac problems is worthwhile, so that possibly the two should be combined somehow.

Thinking about this, if people can use an over-the-counter event monitor system, I am not sure why they can't walk into the corner drugstore and get a 12-lead EKG anytime they want or get a chest x-ray when they have a little cough. I mean there is a lot of those sorts of things that currently now you have to go through a physician to be able to get them.

Does this open up a can of worms, and, you know, that everything now will be, you know, we want to empower patients, and they shouldn't have to go through the nasty physicians to get access to medical care?

I think a lot of things could really fall in that

category, so I think we have to be careful about what we are approving here.

But I think the business about safety and efficacy, I don't think anybody here has any doubt that the device will transmit an arrhythmia. I mean it does transmit an arrhythmia, and it will effectively do so. It is more the system that we are looking at in terms of being safe and effective, and I think it is safe and effective for the worried well who don't need it anyway, and I don't think it is safe for patients who have got serious cardiac problems already. I think they could be doing the wrong thing. I do agree with Dr. Tony Simmons that I don't think a whole lot of the worried well are going to be reassured by this. I have my best chance at reassuring people if I don't want to see the event monitor any more and I tell them to put it away and I tell them not to focus on it anymore.

To have them keep recurringly transmitting these things and focusing on it, I think it just ups their anxiety rather than relieves it.

So those are the only comments I have.

DR. GILLIAM: I agree fully with everything that Dr. Curtis just said. I think if I were going to look at that, I would also take out fainting because, obviously, if someone faints, they can't use this event card. I don't

like any A, B, or C versions. I think some may be better than the others, but the truth is we are looking at a population perhaps suggestive of 10 million people. In my wildest dreams, I don't think I have 10 million people that I would want to have an event monitor.

I guess if we are looking at being safe and effective or efficacious, and I guess efficacious means if there is an arrhythmia, you find it. Well, maybe if I can take some poetic license and say efficacious, do they need the thing in the first place.

I think we can all go out and, say, I could put defibrillators in people, and they are safe and they are efficacious when you choose the right population, and I am not convinced that we have any hope in selecting a population that needs the device.

Just because you give patients access to medical care doesn't mean they get better medical care. I think this is a bad idea. It is not like the blood pressure cuffs. It is not like the pregnancy tests. If someone is pregnant, they sort of know what is going to happen. If I tell them they are going to have, you know, a 20-beat run of v-tach over a telephone, I am not sure they know what happens.

I mean I am not sure I would know that if someone

called me and said they had 20 beats of v-tach out of the blue without me knowing the patient, what I would do with it particularly. We need to know a lot more information.

I think this is a tool. I mean it would be like having Instromedix telling them they could sell the device to anybody who wants to pick it up at their local 5 and dime. It is just that it is a $800 price tag plus 600 bucks, so it means I figure if someone is going to drop $1,500, I think we are going to improve access to care, because if you are willing to spend $1,500 for a device, that we automatically are going to eliminate lethal arrhythmias just for a couple of flutters, you have got a doctor already.

I will stop there.

DR. SWAIN: Dr. Gregoratos.

DR. GREGORATOS: I have one more comment to make for the record, and then I will try to answer some of the questions. It was discussed before, somebody asked whether there is any harm to the device, and the answer was no.

There is one potential aside from everything else that has been discussed, I have one potential concern about anxiety. I think in some people far from alleviating anxiety, this may reinforce anxiety, and I think it has been stated that this may be helpful to anxious people, giving

them sort of some reassurance, some intervention, and I am reminded of the study that just reported at the ACC sessions about three weeks ago on post-myocardial infarction psychologic intervention where people were randomized, part of the group getting nurses calling them to monitor their progress, and so forth, and the other group had the usual and regular care, and the subgroup of the people who got intervened upon with monitoring and regular telephone calls actually did worse. It turned out the women for some reason did worse than the men.

So, when we talk about the psychologic intervention, there are a lot of things we don't understand and we don't know, and there is that potential that is of some concern to me, that may outweigh the benefits that you have listed.

Now, to my way of thinking, a very important issue would be to make sure that the physician that the patient specifies is the appropriate physician and that actually the physician signs off as accepting the responsibility. So I would add to the patient enrollment form that the patient signs, a signoff line by that physician. I think that would be very important. I think that would make it easier for the company also to make sure that things don't fall through the cracks and you don't open yourselves to any liability.

I would also agree with Dr. Curtis. I think the C version with specific bullet type indications and contraindications would be easier for the subscribers to follow than a written narrative type of indication and contraindication.

In terms of the contraindications, I would propose that in addition to history of arrhythmias, as a followup to my previous discussion, the presence of a defibrillator or a pacemaker be considered inappropriate. Those patients would be considered inappropriate for this method, for this follow-up method.

So, Question No. 1, I think we have discussed sufficiently. I would agree with that modification up there.

Question No. 2, I would add defibrillator and pacemaker patients. The labeling will have to be addressed even more. Again, a followup of what I said before, I think a very good subscriber education, a videotape would be very important, expanding on the videotape as you have mentioned before.

Item 4. The provider signoff. I would want to see that as part of any approval. Question 5, I am not sure what that refers to. Were you referring specifically to a pilot study or some type of preliminary process?

DR. SPYKER: If it is determined that there are no appropriate -- or those of you who might feel there are no appropriate patient subsets, then, our next task is to recommend what direction and by what method to pursue that. So, Question 5, if you answer Question 1, then, it is either 2 through 4, or 5 is sort of the way we thought about it.

DR. GREGORATOS: I think with those provisions, I would leave 5 unanswered.

DR. SWAIN: Dr. Tony Simmons.

DR. T. SIMMONS: Well, I guess just trying to answer the question we started on, I agree eliminating fainting. If you are passing out, I don't think that should be on there. I would add congenital heart disease down here because certainly one of the common ways patient with congenital heart disease die is by sudden death. I don't think they should be their own doctors.

I would actually separate those bullets out with coronary disease, valvular heart disease, congenital heart disease, and make those all separate bullets. I think adding, as Dr. Gregoratos said, permanent pacemakers, implantable defibrillators also makes sense.

I think your point about the blood pressure monitoring, just to put my own two cents' worth in on that, and the pregnancy tests, and the HIV testing that can be

done, you know, those patients do buy these kits, they do, they are self-contained, the patient then makes a decision, they do their own determination.

I mean if they want to depend on those things, that is great, but what you are selling here is something that is being interpreted by technicians and partly by physicians and making recommendations on therapy, not therapy, treat, not treat, go to the emergency room or not go to emergency room, and I think that is completely different.

That is all I will say.

DR. SWAIN: Could I ask you what your answer to No. 1 is?

DR. T. SIMMONS: I thought that is what we were doing.

DR. SWAIN: So you are just saying 1 through 4 in arrhythmias?

DR. T. SIMMONS: Actually, strangely enough, I think having just a history of an arrhythmia doesn't exclude you. I am not saying I would agree if you make me vote on this, that I am going to vote yes --

DR. SWAIN: No votes. Dr. Jacqueline Simmons.

DR. J. SIMMONS: Let me just ask a question maybe to staff of the FDA. By looking at C version, under I guess

on the first question, am I eliminating the points under A, like anxiety is a question, athletic, traveling, does that mean that that will not be considered?

DR. SPYKER: Question 1. We must avoid the appearance of leading the panel, and we try to do that by saying if there are, the implied part of Question 1, if there are situations, patient population, where this is appropriate, tell us what they are. You are entirely at your own discretion in terms of including or excluding.

DR. SWAIN: So what parts in A would you want where?

DR. J. SIMMONS: I agree with what I see up to the top. I agree with eliminating fainting, coronary artery disease, and heart failure. That is my answer to Question 1. I agree with 2, I agree with all the points that have been mentioned before. Let me skip to Question 4. I would like to see in the application process where we have physician or institution, I am not comfortable with having the customer assign the institution because it is too broad, and I think it needs to be a provider, you know, a physician involved.

Under 4 also, another modification I would like to see is where the customer is interfacing with the technician, particular when they are referred to the 1-800

number when they call saying they are having these sentinel symptoms, it was my understanding they are going to be referred to the designate provider,and I have a problem with that, particularly if it is something that the patient is to be referred to 411 or, you know, 911 as an emergency.

I think that is it.

DR. SWAIN: Dr. Weintraub.

DR. WEINTRAUB: I just want to state wanting. As a cardiac surgeon, we deal with postoperative arrhythmias fairly frequently, and, in fact, just about the only time we ever call the cardiologists to help us take care of postoperative patients with arrhythmias. Then, we call the EP people, and then I swear they have a dart board in the back room, which has Class I and Class IIA, Class IIB, they blindfold themselves and go like that, and they say, well, use lidocaine or whatever it is, because they probably don't do much better than that.

I am probably a little bit more sophisticated, a little bit, than the average person out on the street, and I often can't figure out what to do with the information, so the whole -- you know, this is just sort of summarizing what everyone else has said -- I am not sure this information is terribly useful, and I sure as hell don't know who the target population is. I can't believe you haven't done

marketing research on this, and all I get right now is a picture of a white, upper-middle-class patient with a charge card is about the only person you are aiming at, and if that is the case, you know, what is the efficacy, as someone has said, he has probably already got a physician.

But having said all of that, and realizing that approval may be likely, I would -- I like the B version if we are looking at labeling, I like the B version, but I understand that the feeling about the bullets on this.

Is it possible to say something to the effect that you might benefit from the use of personal heart device and the Heart Alert monitoring service if you have heart problems related to an irregular heart rhythm and you and your doctor want to be able to test the heart rhythms while you were experiencing symptoms, some symptoms of irregular heartbeat are -- and then the four or five bullets, and then continue with the rest of it?

I think B had a lot of disclaimers and also implies the complexity of the problem, and that is why I sort of didn't want to give it up, sort of combining -- well, in the second paragraph, to enumerate the symptoms.

DR. SPYKER: By no means are these exclusive. We were hoping to get this kind of interchange with you.

DR. SWAIN: Dr. Vetrovec.

DR. VETROVEC: I just want to make kind of a general observation. It seems to me that in health care overall, we are a little schizophrenic. On the one hand, we are saying we are using too much technology and we are told by managed care we ought to use our stethoscopes more and less devices, and now we are making it possible for patients to go buy their own devices, making them perhaps even more accessible.

So, we are telling two different stories. All that aside, I think that this combination of B and C probably makes the most sense. I would agree with the list as it is, and I think a history of arrhythmia is okay to put in, but I feel very strongly that the exclusionary ones that have been listed here ought to be listed, and I really do favor the bullet format, so people can see them easily, particularly things like pacemakers, I think that is real limit to the system.

So, I would suggest that you could this labeling so it is fairly clear what would happen. The last thing is, I think under your Question No. 4, what other comments, I would say very important that physician notification be involved in there somehow, and probably not an institution.

DR. SWAIN: More than notification sign-on or acceptance?

DR. VETROVEC: I am not quite sure how to do it, but I think the physician has to know they are being demarcated for this and has to agree to it somehow.

DR. SWAIN: Okay. Agree to it.

Dr. Gooray.

DR. GOORAY: No questions.

DR. SWAIN: Dr. Goggins.

DR. GOGGINS: Nothing else.

DR. SWAIN: My only two additions, I can't personally select a group of patients that this should be safe or efficacious for, again, because I see no data, but if the FDA actually decided to do this, I think that the contraindications would be people that had a previous EP intervention, ablation or whatever, and in particular, cardiac transplant patients, knowing that simple atrial arrhythmias often portend rejection.

Dr. Simmons.

DR. J. SIMMONS: I was just wondering, shouldn't we also spell out heart attack, because this is for the seventh grade level, right, instead of just saying coronary artery disease?

DR. SPYKER: What was the second --

DR. SWAIN: Cardiac transplant. This has to be rewritten. I think we all agree that writing any patient

instructions are at the sixth grade level. That is what you all go on. And nobody knows what arrhythmias mean. So if this were going to be approved, it would have to be written at the sixth grade level, which actually changes heart failure, people don't know what heart failure is.

DR. SPYKER: If we do wind up with some subset to treat, one or more of you might volunteer to look over the final -- that type of thing is always appreciated.

DR. SWAIN: Gabe?

DR. GREGORATOS: I volunteer.

DR. SWAIN: Oh, okay.

DR. GREGORATOS: But I do have a comment that we ought to address. On the original indications, the issue of persons traveling was listed, being away from contact with the primary physician, I have no problem with that if it is phrased up properly, might be modestly helpful in people who are away from their immediate health care environment, so I would be in favor of working that into the indications.

DR. GILLIAM: We didn't ask the question, but how are you supposed to find out local doctors. If my patient goes to Oklahoma and calls you from Tulsa, how are you going to give him a doctor?

DR. BRILL: We have been assured that there is a way to get into the 911 system.

DR. GILLIAM: You wouldn't call me.

DR. BRILL: Not if they were in Oklahoma.

DR. SWAIN: I guess one question that hasn't been addressed in any of this, and we will ask the FDA to consider in the long run, is the whole electromagnetic question, cellular phone, somebody tries to zip the stuff over cellular phone, and what that does to data integrity and all that. That is an engineering question, I think.

The previous 510(k), the issues were addressed we were told, and we didn't have access to that.

Tom or Dan, do you have the sense? I understand we are not going to have a vote.

DR. GILLIAM: We are not going to vote?

DR. SWAIN: Well, that is what I have been told.

DR. CALLAHAN: The only thing I wanted to make sure is that we distinguish the difference between a procedure we use here versus one we usually use with premarket approval applications. Usually, with the premarket approval application, we have a specific device that is in front of us with data, and we say, okay, is there enough to approve the device or not.

Here, the case is not the approval of the device, but more of the labeling, is it possible to label this device -- which is already out there -- is it possible to

label this device for use by the lay population, and these questions sort of lay out that tenet.

DR. SWAIN: Would it help you at all to have a poll? We have got voting and non-voting members, which doesn't matter, because we are not going to have a device to vote on even though the question is whether this is a system or device. Would you like a poll of yes or no to your question by everybody sitting on the panel, meaning can you label it to make it -- okay. Tony.

And the question is: can you label this device to satisfy the restrictions that you would wish to put on it -- for over-the-counter use?

DR. SPYKER: We agonized over how this question ought to be asked, and Question 1 is really sort of the fundamental question. Are there patients who you think this can be done for safely and effectively? So, that is the way we thought it might be appropriate to phrase it. If the answer is yes, then, we will work diligently to carry out your wishes in terms of labeling, and we will let you, encourage you, in fact, to look at the result. But if the answer is no to this, then, we have got a different set of --

DR. SWAIN: Tony, yes or no?

DR. T. SIMMONS: Say it again. I am sorry. What is the question you are asking?

DR. SPYKER: Are there patients, how would you describe the patient population for whom this system could be done safely and effectively without a prescription?

DR. SWAIN: Can you describe a patient population that this is both safe and effective for?

DR. SPYKER: We have really been asking what would the population be, and now we are sort of asking for a summary of yes or no, are there such patients.

DR. SWAIN: So, the question is, is there a group of patients that this is safe and effective for -- that can be labeled as safe or effective?

DR. SPYKER: To be read by them.

DR. SWAIN: Right.

DR. T. SIMMONS: I would have to honestly say yes, you could define a patient population.

DR. J. SIMMONS: Yes.

DR. WEINTRAUB: Yes.

DR. VETROVEC: Can I ask the FDA a general question in terms of patient empowerment? I mean is there a limit to this? Is the potential in the future for a patient to be able to buy a stent in the drugstore and bring it to me to have me put it in?

DR. CALLAHAN: Things like that are certainly being -- if you look at the Internet, you can see various

things on there already that they are essentially doing that. They may not come in hand with that, but they certainly know what is out there, and they certainly come to you, I am sure, with the suggestion that maybe they need this. So, I would it is a brave new world, we may very well enter into that.

DR. SWAIN: Dr. Vetrovec, do you have an answer?

DR. VETROVEC: Yes.

DR. SWAIN: Dr. Gooray?

DR. GOORAY: No.

DR. SWAIN: Dr. Goggins?

DR. GOGGINS: Yes.

DR. SWAIN: Dr. Gregoratos?

DR. GREGORATOS: Yes.

DR. GILLIAM: No.

DR. SWAIN: Dr. Curtis?

DR. CURTIS: Yes.

DR. SWAIN: No for me.

I think the comment I would have to make about this particular -- the way all this happened, there are some new panel members here. I am very dissatisfied with how we got the data, what order, and I understand that there is issues on the company side, the FDA side, and all this, about whether data was forthcoming and how quickly it was

forthcoming, and all that, but I think it made it incredibly difficult for us to have three sets of things to look at, that kind of -- the target kept moving today.

Likewise, I think many of us very much depend on a cogent FDA summary of a device, questions asked, and some evaluation which we didn't have today. We had questions, but we got those dropped off on our laps at the beginning of the meeting, so you could choose to listen to data or read the questions.

So I think a lot of the sun and the moon were in various phases on this one, that maybe we shouldn't duplicate this effort today.

DR. GREGORATOS: I have a comment. I am a little confused also, a little bit different issues, although I agree with a lot of what Dr. Swain said. I thought we were proceeding to review the labeling indications, and it was part of making specific recommendations, and then in the last 15 minutes, somehow we changed the tack, at least I have a sense of we have changed tack completely, and we are closing this session rather prematurely with a statement that, yes, I think the majority said yes, there can be labeling, appropriate labeling.

I thought it would have been more appropriate and from my experience on these panels many years, it would have

been more appropriate to continue to discuss, to get the panel consensus of what the appropriate labeling would be and then have the panel vote, in fact, that we are recommending or we are not recommending the approval of this device for over-the-counter use with the appropriate changes that we have made. At least I thought that was the process that we have previously followed.

DR. SWAIN: I think Tom explained to me at lunch, which I didn't understand, the difference of today versus any other day.

DR. CALLAHAN: We are not meaning to shut this off at this stage. It is just that the first question essentially says can you define a patient population. If you said, no, you can't, then, there is no sense continuing along that tack, we would go another tack and say, all right, then, how do we go about doing that, do we have to run a pilot study or do we do this.

If you say there is a population that can be identified, who can self-identify themselves through labeling to use this service, then, think you are right, we ought to continue on a bit and see who that population is and how it should be labeled. The more information we have from you, the better off we are.

DR. SWAIN: Tony.

DR. T. SIMMONS: I think certainly when the question was posed, I was answering it as a theoretical question. If you are asking me can we solve those issues based on what is in this packet today, I would say no. I would say there is no way in the world this device should be allowed on the market at the present time. There are so many unanswered questions that are in this packet that I can't even -- there was a lot of agony there the way I had to answer that question, because is it theoretically possible to define a patient population, yes, it is theoretically possible. Can I do it from this? No, I don't think so. I would have to sit down and really think about this a lot.

Also, there are many unanswered questions about the company and how they are going to handle these things, and what is going to happen with the physicians, and who is going to get notified. I mean we could be here for days trying to straighten this thing out.

DR. SWAIN: Jacqueline?

DR. J. SIMMONS: I was a little concerned. I thought that is what we were answering when we went around the room, that was a patient population, but if you are really asking us the latter question, then, I think maybe, I mean I would say no.

DR. SWAIN: Anne.

DR. CURTIS: I think if you went around and asked whether or not we agree or would favor approval of this system for over-the-counter use, I guess we could poll, but I suspect that there would be a lot more negative comments than what you got the first time around, and that is basically the way I feel about it, too.

I could work my way into a very narrow range of patients who, okay, fine, they have got the palpitations, they could document them with the system, and then go to the physician, instead of going to the physician and then documenting them with me.

Is that so important that we get around all these other potential problematic issues about inappropriate use and how do we really guarantee that patients that shouldn't get it, don't get access to it? That really bothers me.

So, I am a little concerned about the very narrow lawyerly interpretation of each one of those points where I could say, well, yes, there is -- yeah, there is a patient population, and not really get at the global issue, which is that I think we all believe this is problematic at present.

DR. SWAIN: Should there be a study or data required before you change you mind, Tom?

DR. CALLAHAN: If that is the way, you probably

need to go around and get a consensus again, but if that is the case, then, we need to be dealing with Question 5 rather than 1 through 4.

DR. SPYKER: Certainly, those of you who voted no, and I think it is appropriate that you first consider the hypothetical, and the hypothetical is, is it possible, is it conceivable, and if you have some specific things that we can do for this particular sponsor in this particular scenario, that is good, too, but particularly those of you who said no, you didn't think it was theoretically possible, then, you need to come back with some suggestions for us, how do they proceed from here.

DR. GILLIAM: I felt no pretty strongly. Maybe that is a challenge to me. I can't envision a patient population that over-the-counter at this time this could be a real benefit for, because we are talking about the patient spending out of pocket close to $1,500, and the vast majority of them it seems that we would never, as physicians, prescribe this for them at all.

I don't see a use for this. I see a great abuse potential. Maybe when it costs 5 to $30, like the pregnancy tests, that sort of throw-away money, maybe I could see it, but $1,500 for something that purportedly is going to protect their heart, to the general population, I don't know

how you can --

DR. SWAIN: I don't think we can focus on the economics. It is very important that we not focus on that.

DR. WEINTRAUB: I just asked that question to try to define a market population.

DR. GILLIAM: I guess the economics isn't making the decision as far as I mean we are in effect, the majority of people, if not all the people, who would end up using this device, it is frankly not indicated for.

DR. SWAIN: As one of the other "no-ers," I think I would have to change my answer to yes, theoretically, yes, put in that terms that there probably is an indication. I would like to see a sponsor bring to me what they thought the indication was, and if they thought it was people with coronary artery disease, and then show me it is safe and efficacious for coronary artery disease, if they think it is the worried well, that you will make then less anxious, then, do a study to show me that they are less anxious, but I have no data, I can make no decision with no data, and I think I would turn it around is prove an indication with data.

DR. GOORAY: I said no. It is implicit in when the FDA puts a stamp of approval, patients don't look at anything beyond that. Patients don't read all these things.

Patients, the FDA says it is okay, then, it must be valuable, and then no price is paid on the value or the benefit.

Although theoretically possible, that is true that I, as a patient, may benefit from this, the avenue in which I am going to benefit from it is so circumferential that it is possible that I am not going to be want to be given that opportunity, there is some problem that is going to create a problem to my own health.

When FDA puts a labeling stamp of approval on something, it has far-reaching implications, and irrespective of all this negative labeling that you put on this, people don't sit down and go through the details of this, they don't.

DR. SWAIN: Any other comments? I think one question that keeps getting ignored is device versus system, we keep getting back to device, but our original charge at the introduction was system, and there is very little system data or even outline of the system here, and that may be an issue that, as we discussed earlier, that you want to convene a group of societies and other outside experts about looking at systems, because that is a new paradigm as far as I am concerned. It is not just simply metal and plastic. It is more answering the question can you make a heart

valve, and then we go by individual heart valves, but this is different and it is difficult.

DR. CURTIS: Another thing, too, I feel like now with the questions that are being asked, that we are being asked to find a way to make it possible to market this thing over the counter, you know, is there any way we can word this, that will make this thing work, and that bothers me, too, exactly because of the issue of no data. I mean we can theoretically think of ways where that might work, but I am not sure I want to be in the position of helping out a company market something over the counter that I don't really believe in anyway.

DR. CALLAHAN: Maybe the question then should be re-posed to go back and say, not theoretically, but all we have is what we have, so maybe the question could be re-posed and say can you label this device for over-the-counter use for the population to be able to make an informed decision.

DR. SWAIN: And the other issue that I think has been brought up by several panel members is that this device has a potential of being unsafe, and I know the spin that is going to come out of it as you are not letting patients take care of their own care, and that can be the front page, as somebody said, of the Washington Post, but I think from my

personal view and what I hear from other panel members is that there is a real opportunity to harm patients with this device, so the spin shouldn't come off we are taking patients' empowerment away. This is protective.

MR. COSTELLO: Do I get a chance to say anything?

DR. SWAIN: Any other panel members or does the FDA have any other --

DR. CALLAHAN: Only if you want to clarify the poll, whether it is theoretical versus what we have to deal with.

DR. SWAIN: So you want two questions, theoretical versus actual, theoretical versus this system.

DR. CALLAHAN: We are going to have to sit down and draft a label within the next week to make a decision on this if you think it is possible to do. So we would like, if you think it is possible, some guidance as to what that population is and how we can best communicate that information. If it is not possible, then, we would like to have that information.

DR. SWAIN: Not possible meaning somebody wanted data, more data or something?

DR. CALLAHAN: Not possible to do.

DR. SWAIN: Dr. Spyker.

DR. SPYKER: I do feel I want to respond to Dr.

Curtis' comment because we agonized over how to phrase these questions, and please accept my statement that we did not intend these questions to say please approve this at any price. We simply were trying to say don't throw the baby out with the bathwater, if there are some values to this, then, tell us what the values are, and we who agonize with labeling for a living will probably be able to cook up something to make it accurately reflect your needs.

We are not by any means trying to sway the panel in that direction.

DR. SWAIN: We are limited on time and we need another full session. Does anybody not understand the -- as far as I can tell, the two questions that are being asked: a theoretical question about could you ever do this, and an actual question about --

DR. SPYKER: Have we done it?

DR. SWAIN: Have you done it, exactly.

DR. GREGORATOS: No, no, no.

DR. SWAIN: Gabe.

DR. GREGORATOS: We certainly have not done it, but the question is really -- the actual question is on the basis of the available data, could you do it as opposed to theoretically, which would require additional data. At least that is the way I look at is.

DR. SPYKER: The question is additional data or not, and if we need additional data, then, that is what I mean we haven't done it, in other words, with this package, with this submission.

DR. SWAIN: Do you feel that there is no possibility any additional data would ever make you agree you could do this? That is one question. And on this one, could it be done with additional data or is there adequate enough data now to do it. That is as close as I can get to this.

DR. VETROVEC: By "additional data," you mean in some way modifying what the company says, the sponsor says there is going with it, is that right, or how they are going to handle it?

DR. SPYKER: The distinction is things we can handle in labeling, and in labeling I include things like the triage physician, like you have got to have a signoff by a doctor. That is something that I heard a number of times, and it seems to make sense to me. So, that is something that I believe is within our power. We do have a good deal of regulatory authority to make that kind of thing happen, but we do have -- I mean things we do in a week, and in a week we can't run a study to find out whether the walking wounded are indeed going to be helped with this or whether

there are patient who are going to die as a result of delay, those are things we can't do in a week, so that is the distinction I am trying to make.

DR. SWAIN: Dr. Gilliam.

DR. GILLIAM: I have sort of a leading question. Can I sell a patient of mine one of these devices? I mean the patient comes to my office, is my patient, can I say, okay, for 1,000 bucks you have the device, and I will monitor him? I mean is that legal?

DR. CALLAHAN: Right now you can --

DR. SWAIN: I don't think that is a question that we want --

DR. GILLIAM: I mean the reason being is I am just trying to get at some understanding of what we mean by the system. If we said we could theoretically do this, I mean does it mean anyone on the street?

DR. SWAIN: No. We are just looking at over-the-counter use for this device.

DR. GILLIAM: Okay.

DR. SPYKER: Which is already up and running in a prescription mode.

DR. SWAIN: Yes.

DR. CALLAHAN: I think the only confusion came, and it was confusion what was brought out, but Tony

mentioned or Dr. Simmons mentioned that he voted on the theoretic base that, yeah, there could be some way of doing this, but our problem, as Anne is alluding, is do we have that possibility now in front of us, so we are trying now to distinguish between when we went around before saying can we do this, the idea was can we do this with what we have. All we have is what is in the submission. So we are trying to make the distinction now, not on a theoretic basis, but can we do it with what we hand in hand.

DR. SWAIN: Okay.

DR. T. SIMMONS: I would say, you are asking me for my vote --

DR. SWAIN: Your view -- we are not voting -- view for the FDA.

DR. T. SIMMONS: My view is that it is conceivable to theoretically define a population. There is no way on this submission, no way.

DR. SWAIN: Dr. Jacqueline Simmons?

DR. J. SIMMONS: I think about 20 minutes ago we went around the room and we talked about the group, changing from B to C, and I think that it was my understanding that is a population base that we could market this to, and so I think the answer to that would be yes.

DR. SWAIN: In the next month, do you think the

data is sufficient to make that answer yes now for this particular device versus a theoretical?

DR. J. SIMMONS: Not really.

DR. SWAIN: So does your answer agree with Dr. Simmons, yes and no, yes theoretically?

DR. J. SIMMONS: Yes and no, right. Yes theoretically and no, we do not have the data.

DR. SWAIN: I don't want to lead you, but in a week do you have the data to do it.

Dr. Weintraub.

DR. WEINTRAUB: The theoretical question until you define that population to my benefit, yeah, I think maybe so, I am not sure what that population is. I am not sure in the long run how important it is, frankly.

The second question about the data, I am not sure that any data would be available no matter what you did. We are talking fairly small hit rates in terms of at best 10 percent in a selected population. This is an unselected population. You are talking about 1 or 2 percent hit rate, and you are going to have to have 10,000 patients before you can prove anything. So, I think the data are not there, the data will probably never be there. I think one has to make the decision on the basis of whether you think this is a harmful device, whether you think it might be somewhat

efficacious in some population.

I don't think the data are there, I don't think they are obtainable.

DR. SWAIN: Would the Class I, II, and II AC recommendations be a backbone to go on?

DR. WEINTRAUB: Probably.

DR. SWAIN: Dr. Vetrovec.

DR. VETROVEC: I think, no doubt theoretically, you can construct a population. Is the data here? I am fairly comfortable with the list that we came up with that it is safe. Is it effective, I don't think we know that at all. I have to agree with Mr. Weintraub I think to prove it is effective would be probably an unrealistic study.

DR. SWAIN: Dr. Gooray.

DR. GOORAY: I think I have said enough.

DR. SWAIN: Dr. Goggins?

DR. GOGGINS: I think I will abstain based on the fact that I don't get a complete package, and I am not a practicing physician.

DR. SWAIN: Dr. Gregoratos.

DR. GREGORATOS: My answer is yes and yes, and I agree very much with Dr. Weintraub. I think that there is enough information available currently to construct a list of indications for the over-the-counter marketing of this

device that would avoid harm. I also agree that probably the benefit to be gained from such marketing is going to be very, very small, if any. And I agree very much that it is well nigh impossible to plan long-term trials that will adequately provide us with additional data.

DR. SWAIN: Dr. Gilliam.

DR. GILLIAM: I agree with everything he said and I will vote exactly opposite, no and no.

DR. SWAIN: Dr. Curtis.

DR. CURTIS: I think I might be able to summarize the answers to the questions. I think what it comes down to is can you describe the patient population. I would say yes, no known structural heart disease with the indications that we have. I think that group of patients it would probably be safe for, I don't think we are going to do anything bad to them.

Is it effective? Occasionally. I think the cost effectiveness is not going to be there, but that is not what we are being asked, but I think occasionally, it could be effective.

In terms of who it shouldn't be used for, I would throw out the patients with known structural heart disease, pacemakers, ICDs, previous EP evaluation, as mentioned, heart transplants. Throw out the people we already know

have cardiac disease. If they have got known cardiac disease, they ought to have a physician, and that physician ought to be better qualified to know whether or not an event monitor is an appropriate way to evaluate whatever symptoms they have.

Thirdly, the labeling. If you modify the B and C, and somehow combine them, I think you could get a list of indications and contraindications that would make sense, and then the further modifications would be to the M.D. agreeing to be a physician of record or those comments that were made, and that the patient protocols be clarified as to what the patients are going to be told and how that information is going to be used, because that has been completely vague so far.

So as much as I overall am negative about the thing, if you ask me can you do it, I would say yeah, in a very selected patient population I think you can make it work.

DR. SWAIN: I wonder if the FDA would like to consider what we did on the short stent, sort of fast-tracked it in a huge change. The original thing was you could put a stent in anybody as far as I recall what that original one was, and that we had a group of experts work with the FDA and the company over a couple months,

perhaps with Dr. Curtis, very much limited, down from 10 million to worried well, people without any evidence of disease, whether a subcommittee of this group with particular expertise could work with the FDA and the company to make it a "yes/probably" rather than a yes/no, which several of us would go for right now. How about a compromise on that one?

DR. CALLAHAN: I think we could do that, but not in a couple of months, it would be more in a couple of weeks turnaround.

DR. SWAIN: Who is defining a couple of weeks?

DR. CALLAHAN: Well, we, in the agency, have had this -- this came through as a 510(k) originally and only recently has the question of, well, can you really label this adequately come up, and so we are trying to, in bringing this forward to the panel, make a decision timely even though we have already had our 90 days to make the decision.

DR. SWAIN: I would imagine that if the company agreed that it was going to be on a longer time line, because it may be that if you had to say a couple of weeks, the answer would have to be no, but, in fact, if the company agreed that it could be as expeditious as we can get stuff done, which is a couple of months, two, three months it took

on that stent, but the company got a product that was refused otherwise.

DR. WEINTRAUB: But wasn't that also pending some national study?

DR. SWAIN: No, it was pending really limiting things. I don't know if that is -- if you have all got the sense --

DR. CALLAHAN: You could poll the company and ask whether or not they --

DR. GILLIAM: I get the sense that we are being sort of asked to endorse over-the-counter use or not, I mean in some way, and I guess I for one would like to say that, you know, we have no data from the company that this is even possible in any way. They say the device is safe. Well, we knew that already. And then it is useful, well, we know that already under a physician's guide, but we have absolutely no information whatsoever.

And if the question is can we do this as an over-the-counter, and you need to answer two weeks from now, I would vote that if you pushed me today, I would say no, you can't. Am I misinterpreting?

DR. CALLAHAN: No.

DR. CALLAHAN: Because I didn't get that sense until just this very moment that we are sort of under a gun

of a couple of weeks to say yea or nay to an over-the-counter -- the real question is can we do this over the counter.

DR. CALLAHAN: That is the real question, but the couple of weeks is only that we don't have any more data, we are not going to have any more data if we wait a month of two months. If you want more data, we have to know what data you want, and then we can decide how long it is going to take.

DR. SWAIN: I think the question came with what Dr. Weintraub and Vetrovec and Gregoratos said is if, in fact, the only indication is the worried well, maybe the agreement would be you wouldn't need further data; if you made an indication for anything other than the worried well, anybody with any kind of structural heart disease, then, you would probably need data. So that may be the question that you will want to consider when you take this under advisement since we are the advisory committee.

DR. J. SIMMONS: Then, that would eliminate that group that we just identified in B and C.

DR. SWAIN: History would eliminate it. We are talking about worried well like starting an exercise program or something.

I just wonder, if there is no more comments from

this group, if the company representatives wanted to comment on something.

DR. BRILL: I wanted one clarification on what you were just discussing. If you require a physician to sign off, and the patient has those things which you are concerned about, but the physician signs off, how does that fit in with the discussion you just had?

DR. SWAIN: You have already got a physician referral service, physician, but --

DR. BRILL: So if the physician signs off, even though they may have one of the things that this panel is concerned about, that is okay?

DR. SWAIN: No, it is not okay. Signing off is far different from being the physician referral arrhythmia service that is present now.

Did you have --

MR. COSTELLO: Yes, I had one quick comment to make before. Many of you have referred to lack of data. Sent to the FDA over a month ago was our historical data referenced in a December 16th memo, and I was curious to determine whether or not that was in your packages at all.

DR. SWAIN: Data on using the other service?

MR. COSTELLO: Data on Heart Alert's current physician-based subscriber service.

DR. SWAIN: I wouldn't think that is relevant, but I don't think it is in the package.

DR. WEINTRAUB: 510(k), it is relevant.

DR. SWAIN: Again, it is a device versus a system. That only says whether that metal and plastic works, not whether the entire rest of the system works.

DR. J. SIMMONS: Yes, we have got that.

DR. SWAIN: You mean the historical data, yes.

DR. BRILL: Is there some data which you conceive we would have had about a subscriber-based service? I agree with some of the doctors who say we might not ever be able to obtain it, but certainly without approval to do it, it would have been difficult to present you with data about how successful it was.

DR. GILLIAM: I think it would be possible to sort of in a limited way test it out and see. I would be kind of curious to see if you stuck it, a free monitor, let's say, in an office of a primary care doctor, just basically say, okay, we are not going to refer anybody to it, just arrange to, say, where you would just see who would pick it up and who would use it, and you would have a lot more information on it, so that is not quite the same, just to have some idea of what percentage of the people walking through the doors and saw it would use it, and who those people would be.

That is not quite the same as $1,500 down.

DR. SWAIN: I think we could go through a whole deal on this. I mean there were six patients as far as I can tell that were mentioned that were in the study. I mean this is so confusing that -- I don't know, and I think we absolutely cannot talk about money on this panel on the financial things. We cannot do that.

Any other questions that the panel has or the FDA has?

DR. SPYKER: Could I get those folks who, should we decide to proceed with labeling this, would be happy to help us review the label?

DR. SWAIN: Who would like to? Dr. Gregoratos would like to do that. I am sure Dr. Curtis would like to do it. And Dr. Gilliam. We have got pretty well the spectrum of views right down this row here. That is not a bad selection for advice.

DR. SPYKER: Thank you.

DR. CALLAHAN: Thank you very much. It is not an easy task, and we struggled obviously with it as well. It is not our typical way of doing business and a typical issue that get brought before us. So I appreciate your struggling with it. We will keep you informed. I think we have an idea of where you all are coming from and why. We will keep

you informed as to where it goes and what the next steps are.

DR. GREGORATOS: But I have a sense that this will be coming down more and more over the next few years, so it may be well worthwhile for the agency to figure out the process like which over-the-counter use of devices is approvable or not maybe a little bit better or figure out what process is going to follow, so we don't run into this quandary every time.

DR. CALLAHAN: That is probably well, and I think what you are finding and what has been alluded to here, it really goes into a whole host of issues like practice of medicine, well care payment, all the new ways of doing of health plans, professional societies. There are big issues here with full swings in the way we deal with medical care. So, it would be well to -- I think you are right, we will see more of this type. I don't know if we will see catheters, but we might.

DR. SWAIN: We are adjourned.

[Whereupon, at 2:44 p.m., the meeting was adjourned.]